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# VASCULAR SYSTEM OF THE HUMAN SPINAL CORD

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This report is that of a study made on a number of human spinal cords by means of postmortem injection or by the benzidine stain. In a review of the literature, we found an interesting fact. Most of what has been written in the past forty years about the circulation of the human spinal cord, especially in anatomic and neurologic textbooks and handbooks, is either inaccurate or incomplete. A paper that gives an accurate and complete account is that by Kadyi,[1] published in 1889, a truly masterful piece of work. He pointed out that only one fourth of the nerve roots in man are accompanied by segmental arteries which contribute significantly to the circulation of the spinal cord; on the average there are but eight. The largest is one in the upper lumbar portion of the cord, the arteria radicalis anterior magna, first described by Adamkiewicz [2] in 1882. In addition, Kadyi established the important fact, which has been overlooked in most anatomic and pathologic texts, that the anterior central arteries (the arteriae sulci of Adamkiewicz [2]) for each side of the spinal cord at any given level originate as independent branches from the anterior arterial trunk or as a short common trunk. Only in the lumbar and the sacral portion of the cord are there occasional instances in which the trunk is common throughout the entire length of the anterior sulcus and splits into a left and a right artery in the depth of the anterior sulcus. In most instances, however, the central arteries are

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1. Kadyi, H.: Ueber die Blutgefässe des menschlichen Rückenmarkes; nach einer im XV. Bande der Denkschriften der math.-naturw. Classe der Akademie der Wissenschaften in Krakau erschienenen Monographie, aus dem Polnischen übersetzt vom Verfasser, Lemberg, Poland, Gubrynowicz & Schmidt, 1889.

2. Adamkiewicz, A.: Die Blutgefässe des menschlichen Rückenmarkes: II. Die Gefässe der Rückenmarksoberfläche, Sitsungsb. d. k. Akad. d. Wissensch., Math.-naturw. Cl. **85**:101-130, 1882.

already separated throughout the entire depth of the anterior sulcus into arteries for the left side and those for the right. They overlap frequently and thereby in transverse sections give the fallacious appearance of splitting. The central arteries are irregular in distribution; sometimes both enter at the same level, but more frequently either a left or a right artery enters at any given level. They do not alternate regularly. Also, their width varies; the largest are in the cervical region, while in the lumbar region they are smaller but more numerous. Altogether, there are about two hundred.

In 1908, Tanon [3] carried out an interesting study by making injections into the human spinal cord from the various levels. He found that from the lumbar vessels injections can be made easily into the entire cord. In the thoracic portion, above the ninth segment, injections from any of the segmental branches can be made only into small stretches. In the cervical segments the territory of each artery is slightly larger.

## MATERIAL AND METHODS

This study was based on 26 presumably normal human spinal cords, obtained at autopsy. The distribution of the arteries and veins on the ventral, dorsal and lateral surfaces was studied immediately after the removal of the spinal cord, and diagrams were made. Subsequently, in 21 cases injections into the cord were made with a dispersion of 1 part of india ink in 3 parts of a dilute solution of formaldehyde U. S. P. (1:10). In 12 cases injections into the anterior spinal arterial trunk (anterior spinal artery) were made from the sacral region near the conus. From this level satisfactory injection into the entire sacral, lumbar and thoracic portions of the cord can be obtained. Injections into the cervical portion usually cannot be made from that region except in young children. An exception occurred in the case of a young adult. In 6 other cases injections into the anterior spinal venous trunk (anterior spinal vein) were made from the sacral region in the same way. In 3 cases injections were made simultaneously into the anterior arterial and the anterior venous trunk. Usually, from 20 to 40 cc. of the injection material was used. In a few cases 60 cc. was used, but the injection was partially unsatisfactory, owing to perivascular extravasation. In a newborn infant 10 cc. was injected. After injection the specimens were hardened in a dilute solution of formaldehyde U. S. P. (1:10). Later the gross appearance of the injected vessels was studied again, and the diagrams were completed in accordance with the observations after injection. Thick frozen sections (from 200 to 400 microns) were cut at various levels, partly in series. They were dehydrated and mounted as usual.

In 5 cases the gross distribution of the vessels was studied without injection and the intrinsic vascular pattern with the benzidine stain (Doherty, Suh and Alexander [4]).

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3. Tanon, L.: Les artères de la moelle dorso-lombaire: Considérations anatomiques et cliniques, Thesis, Paris, no. 98, Paris, Vigot Frères, 1908.

4. Doherty, M.; Suh, T. H., and Alexander, L.: New Modifications of the Benzidine Stain for Study of the Vascular Pattern of the Central Nervous System, Arch. Neurol. & Psychiat. **40**:158-162 (July) 1938.

## RESULTS

As in the brain (Alexander and Putnam [5]), the arterial and venous vascular system of the spinal cord, including the capillaries, can be divided into seven categories, based on the order of relative magnitude. The largest spinal vessels, those of the seventh order, are the intervertebral arterial and venous branches. The vessels of the sixth order are the anterior and posterior radicular arteries and veins and their anterior and posterior anastomoses (trunci arteriosi and venosi). They measure from 1,122 to 340 microns. The vessels of the fifth order are, as in the brain, the meningeal ramifications of the large arterial and venous trunks. The vessels of the fifth order include the common anterior sulcal trunks (fig. 1) and their ramifications, the anterior sulcal arteries and veins, as well as the large

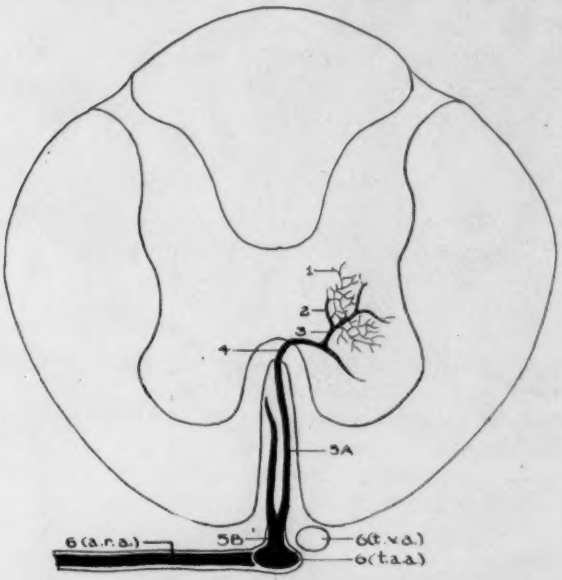


Fig. 1.—Schematic diagram illustrating classification of the spinal vessels in man according to order of magnitude. *1* indicates capillary network (vessels of the first order); *2*, immediate precapillary (vessel of the second order); *3*, vessel of the third order; *4*, vessel of the fourth order, in this instance a paracentral vessel; 5 *A*, a sulcal vessel, for the right side; 5 *B*, a short common trunk of sulcal vessels; *6* (*t.a.a.*), a vessel of the sixth order, in this instance the truncus arteriosus anterior; *6* (*t.v.a*), the truncus venosus anterior, and *6* (*a.r.a.*), the arteria radicularis anterior.

and small meningeal surface trunks. It may be expedient in the spinal cord to divide the vessels of the fifth order into two subgroups, 5 A and 5 B. Group 5 B includes the common anterior sulcal trunks whenever they are present (most of

5. Alexander, L., and Putnam, T. J.: Pathological Alterations of Cerebral Vascular Patterns, A. Research Nerv. & Ment. Dis., Proc. **18**:471-543, 1938.

them are short; fig. 2) and the large surface trunks. Group 5 A includes the sulcal arteries and veins (fig. 3) and the small surface trunks. The range in size of vessels of group 5 B is from 400 to 100 microns. The arterial vessels of group 5 A measure from 72 to 60 microns; the veins, from 160 to 60 microns. The vessels of the fourth order are the largest branches that first penetrate the substance of the spinal cord, such as the paracentral arteries (fig. 4). The size of the arterial vessels of the fourth order varies from 60 to 24 microns; that of the venous vessels, from 80 to 24 microns. The vessels of the third order are the branches resulting

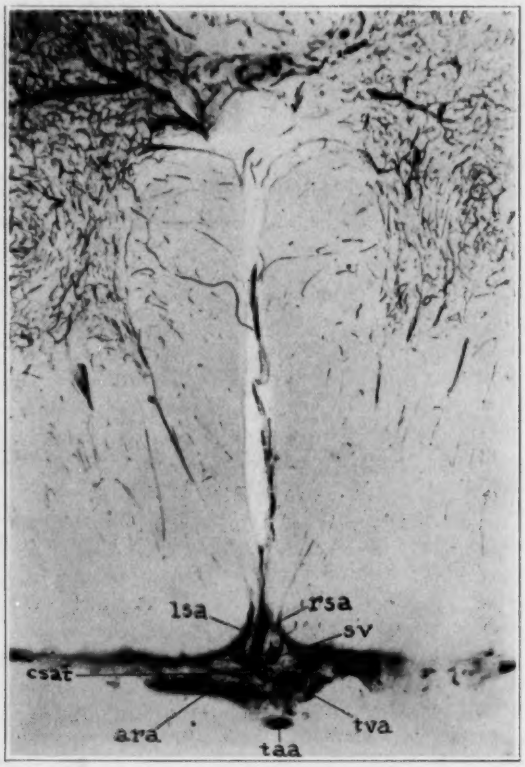


Fig. 2.—Photomicrograph of the vessels of the anterior sulcus of the spinal cord in a normal human adult. Second lumbar segment. Here, *ara* indicates arteria radicularis anterior (left); *csat*, the short common sulcal arterial trunk; *lsa*, the left sulcal artery; *rsa*, the right sulcal artery; *sv*, the sulcal vein; *taa*, the truncus arteriosus anterior, and *tva*, the truncus venosus anterior. Benzidine stain; enlargement, about 23 ×.

from the first intramedullary divisions. They measure from 32 to 16 microns. The vessels of the second order are the immediate precapillaries, which measure from 12 to 8 microns. The vessels of the first order are the capillaries. Their average caliber is 6 microns (fig. 4; table 1).

As already implied, there is a great deal of variation in the size of blood vessels within the various groups determined by the category of the order of subdivision. The differences are most striking in group 6, namely, among the segmental radicular arteries, which join the truncus arteriosus anterior of the human spinal cord (table 2). These arteries are by no means of equal or similar size, as has frequently been assumed, but are differentiated into large and small arteries. As large or significant arteries we regard those larger than 250 microns; as small or insignificant, those smaller than 250 microns. The range in caliber of the large

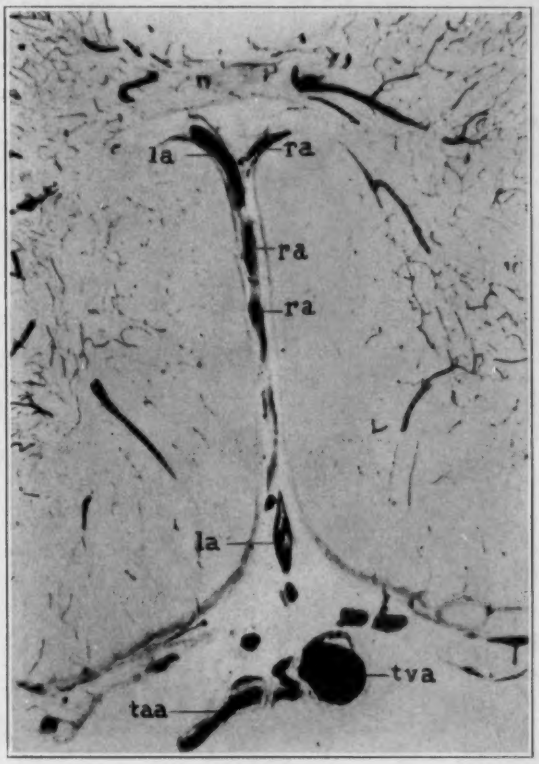


Fig. 3.—Photomicrograph of the vessels of the anterior sulcus of the spinal cord in a normal human adult. Third lumbar segment. Here, *la* indicates the left sulcal artery; *ra*, the right sulcal artery; *taa*, the truncus arteriosus anterior, and *tva*, the truncus venosus anterior. Benzidine stain; enlargement, about 23 ×.

radicular vessels extends from 340 to 1,122 microns; these are the vessels which alone can be regarded as true vessels of the sixth order, as far as the intraspinal circulation is concerned. The range in caliber of the small radicular vessels extends from 34 to 214 microns; these vessels do not contribute significantly to the intraspinal circulation, most of them exhausting themselves about the roots. There are usually only from six to eight large anterior radicular arteries, and it is on these that the spinal cord depends largely for its blood supply (figs. 5 and 6 *A*).

Their distribution is not symmetric. There are usually one or two in the lumbar region, one in the lower thoracic region, none or one in the middle thoracic region, one or two in the upper thoracic region, one or two in the lower cervical region and one in the upper cervical region. The largest is usually the one in the lumbar or lower thoracic region, namely, the arteria radicularis magna. This artery measures 872 microns in the adult and 748 microns in the newborn. This artery is single, not symmetric, and occurs on one side only, more often the left. Its

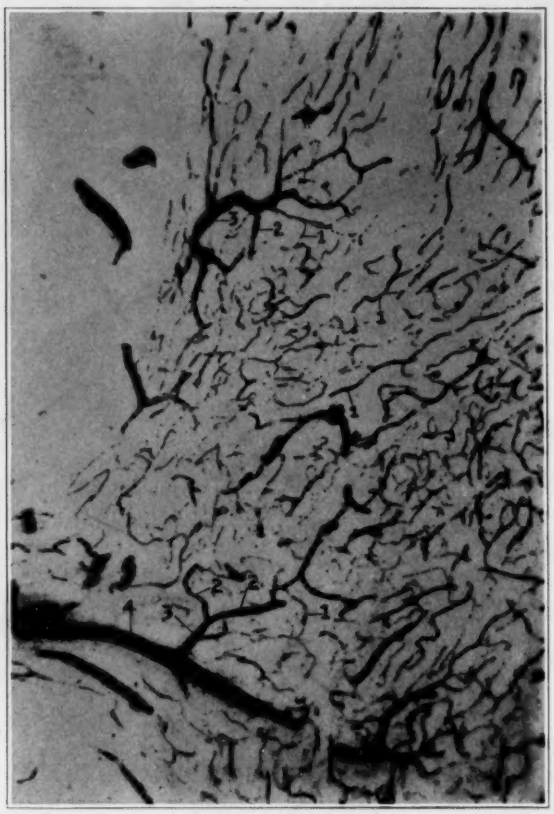

Fig. 4.—Photomicrograph showing classificaton of the intraspinal vessels in a normal human adult according to the order of magnitude. Central part of the gray matter of the third lumbar segment. *1, 2, 3* and *4* indicate the relative order of magnitude (compare with the diagram in fig. 1). Benzidine stain. Enlargement, 47 ×.

most frequent site is the second lumbar segment, but it may be observed at any segment between the eighth thoracic and the fourth lumbar. Kadyi found it between the ninth thoracic and the third lumbar segment. The anterior radicular arteries next in size are those in the cervical and the lower thoracic region, provided the lumbar region contains the arteria radicularis magna; they measure

from 510 to 578 microns in the adult and from 306 to 476 microns in the newborn. In the cervical region they may occur at the third, fourth, fifth or sixth segment. The large segmental arteries in the upper thoracic region measure 374 microns in the adult and 272 microns in the newborn. They may be observed between the first and the third thoracic segment. In the middle thoracic region large segmental arteries are absent in many cases; in others one is present, most frequently between the fifth and the seventh segment; it is comparatively small,

TABLE 1.—*Range in Caliber of Spinal Vessels in Man*

| Relative Order of Magnitude | | Caliber in Microns |
|---|---|---|
| Seventh order | Intervertebral arteries | 500–2,000 |
| Sixth order | Significant radicular arteries and anterior spinal arterial trunk | 340–1,122 (the insignificant radicular arteries: 34–214) |
| Fifth order | B: Common anterior sulcal trunks and large meningeal surface trunks | 100–400 |
| | A: Anterior sulcal vessels and small meningeal surface trunks | 60–72 (veins up to 160) |
| Fourth order | Penetrating vessels | 24–60 (veins up to 80) |
| Third order | Middle-sized intramedullary vessels | 16–32 |
| Second order | Immediate precapillaries | 8–12 |
| First order | Capillaries | 6 |

TABLE 2.—*Number and Caliber of the Spinal Arteries of the Sixth Order in the Various Regions of the Spinal Cord in Man*

| | Region of Spinal Cord | Number of Significant Anterior Radicular Arteries | Diameter of Significant Anterior Radicular Arteries, Microns | Diameter of Anterior Arterial Spinal Trunk ("Anterior Spinal Artery"), Microns |
|---|---|---|---|---|
| Adult man | Upper cervical | 1 | 510 | 510 |
| | Lower cervical | 1 | 578 | 442 |
| | Upper thoracic | 2 | 374 | 374 |
| | Middle thoracic | 1 | 340 | 340 |
| | Lower thoracic | 1 | 510 | 578 |
| | Lumbar | 1 | 872 | 1,122 |
| Newborn human infant | Upper cervical | 1 | 476 | 374 |
| | Lower cervical | 1 | 306 | 442 |
| | Upper thoracic | 1 | 272 | 342 |
| | Middle thoracic | 0 | ... | 272 |
| | Lower thoracic | 2 | 476 | 374 |
| | Lumbar | 2 | 748 | 600 |

measuring only 340 microns in the adult and 170 microns in the newborn. The small, insignificant radicular arteries measure from 34 to 214, most of them from 136 to 214 microns in the adult and from 68 to 80 microns in the newborn.

The truncus arteriosus anterior is made up of a chain of anastomoses, established by anastomosing ascending and descending branches of the radicular arteries. It shows numerous deflections and angulations and is not everywhere placed strictly in the midline; Kadyi explained this on the basis of its originally paired embryonic anlage.[6] The width of the truncus arteriosus anterior varies greatly; one set of

6. Kadyi,[1] p. 65.

variations is roughly correlated with the width of the significant anterior radicular arteries. The truncus arteriosus anterior is largest in the lumbar region (1,122 microns in the adult and 600 microns in the newborn); next in size are its upper cervical and lower thoracic parts (from 510 to 578 microns in the adult and 374

Fig. 5.—Anterior view of the spinal cord of a newborn human infant after injection of a mixture of india ink and solution of formaldehyde into the anterior spinal arterial trunk. Note the remarkable differences in size of the anterior radicular segmental vessels.

microns in the newborn); next are the lower cervical and upper thoracic parts (from 442 to 374 microns in the adult and from 442 to 342 microns in the newborn); the middle thoracic portion is the narrowest part of the anterior arterial

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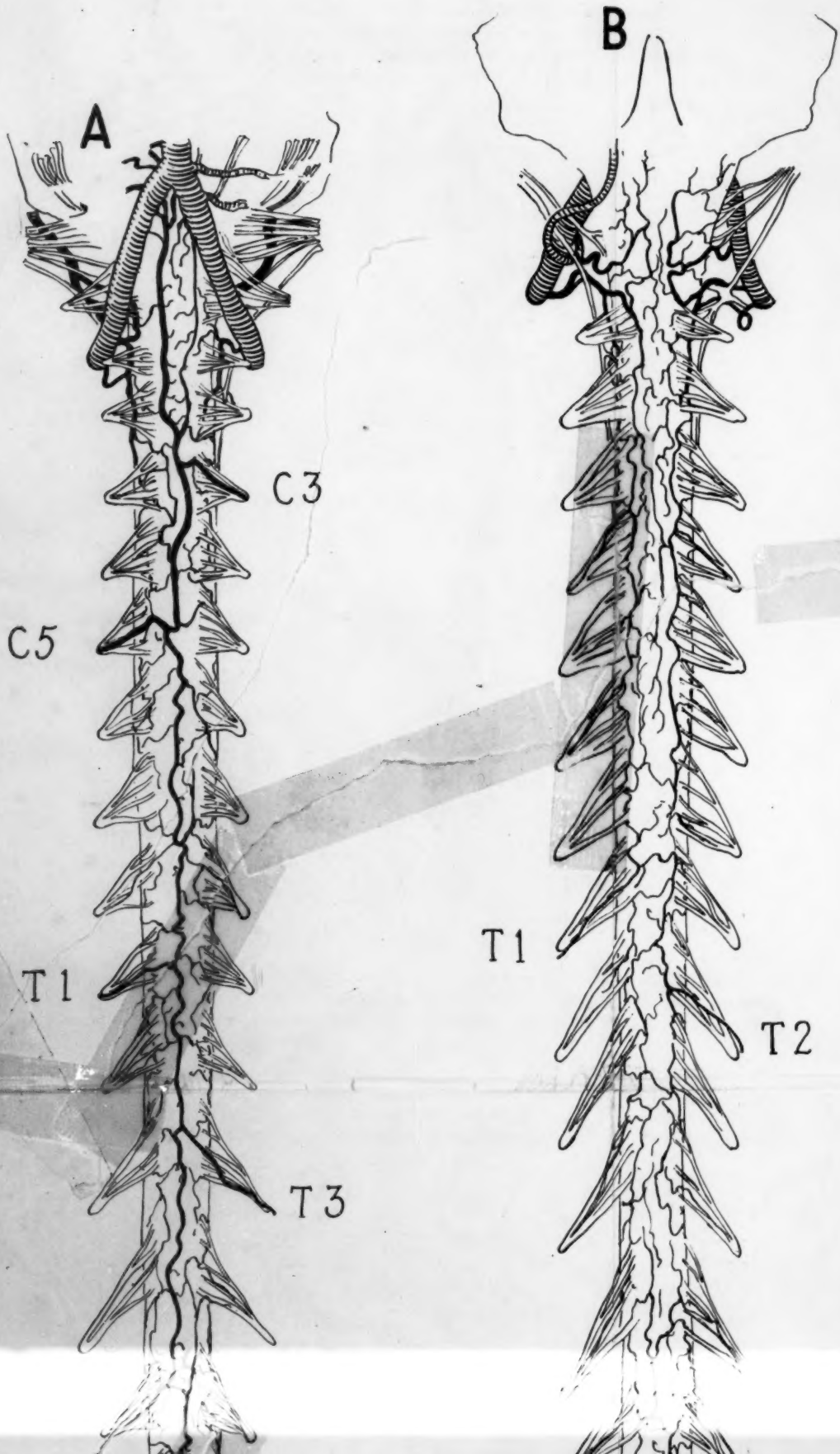
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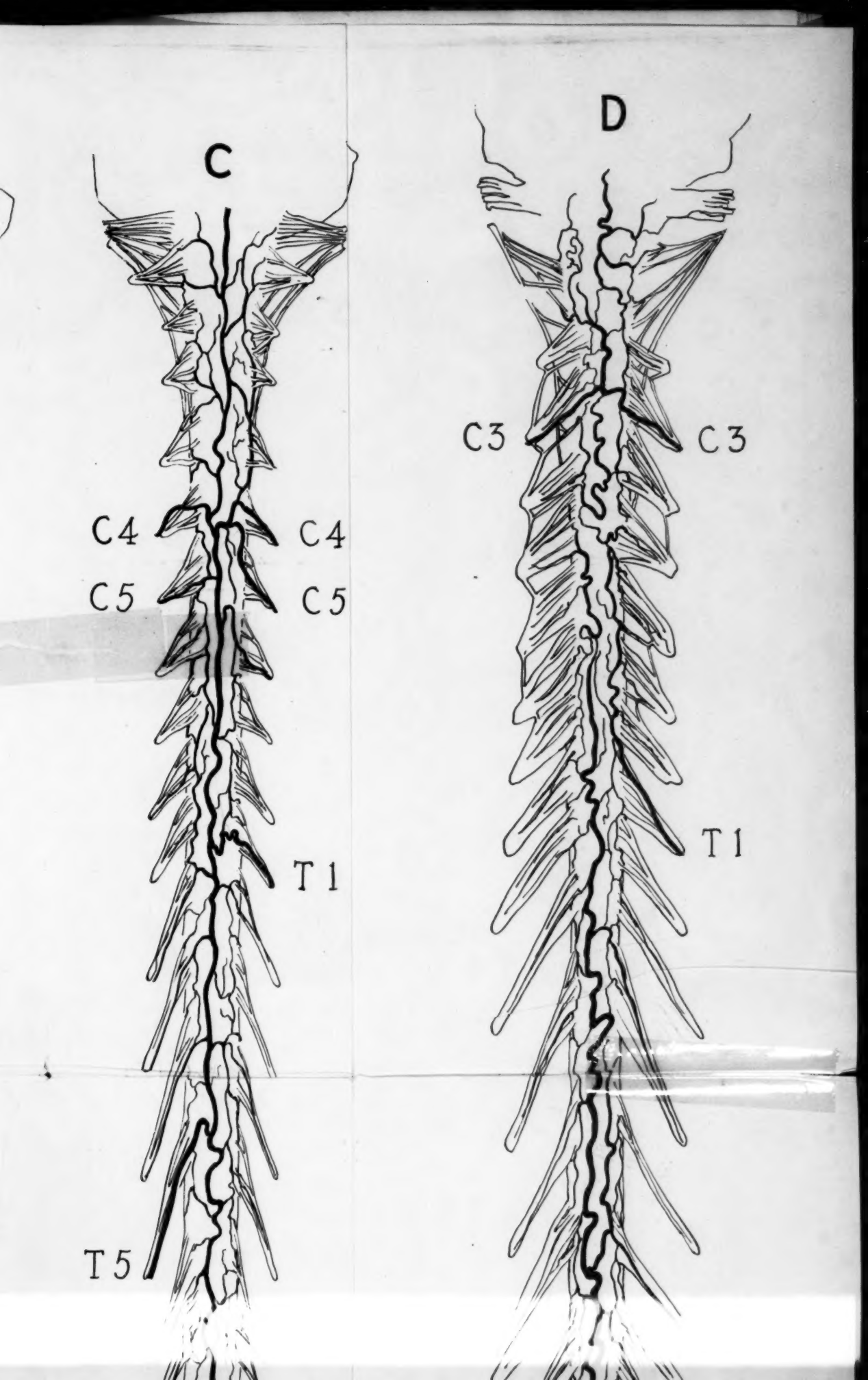
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C3
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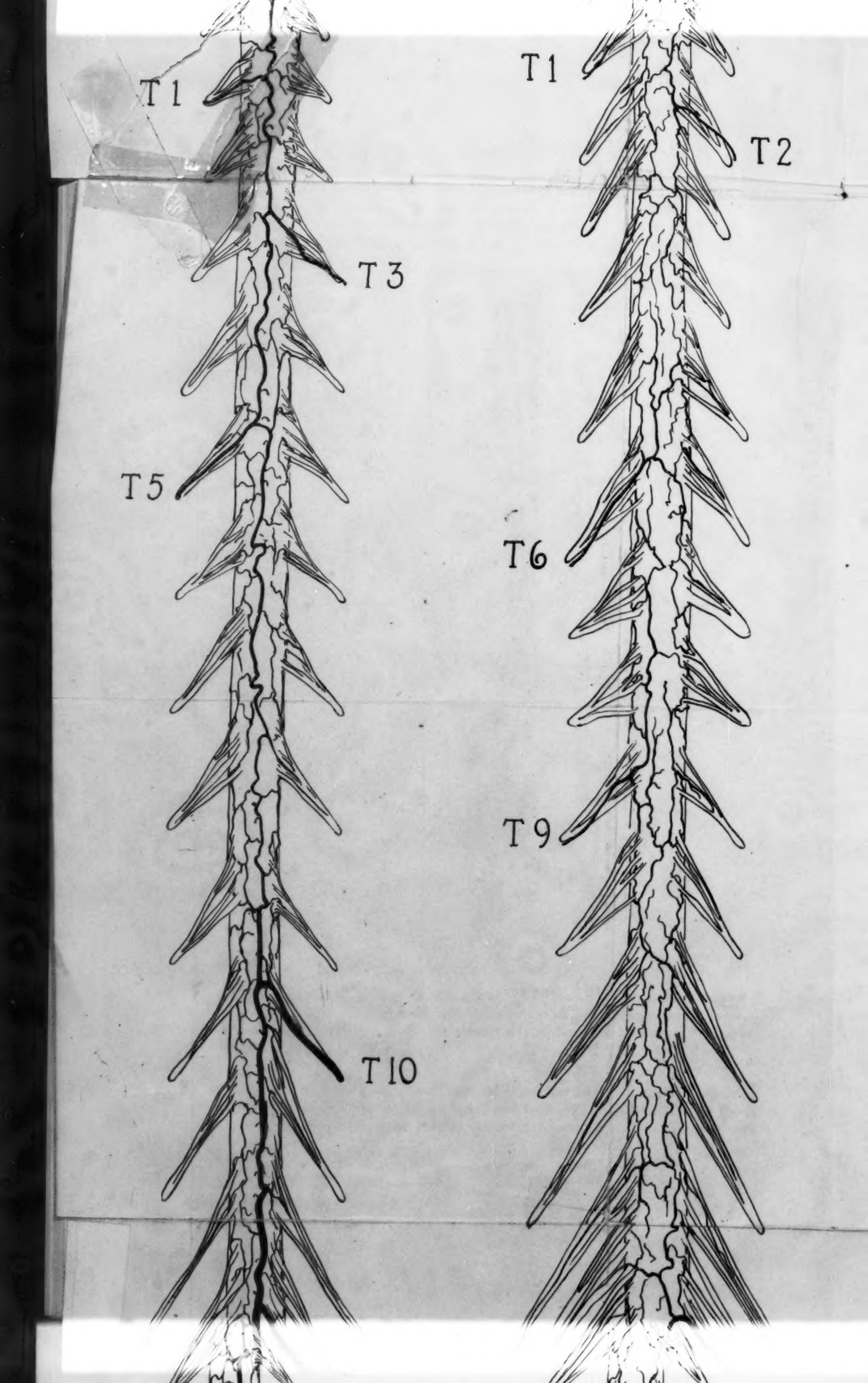
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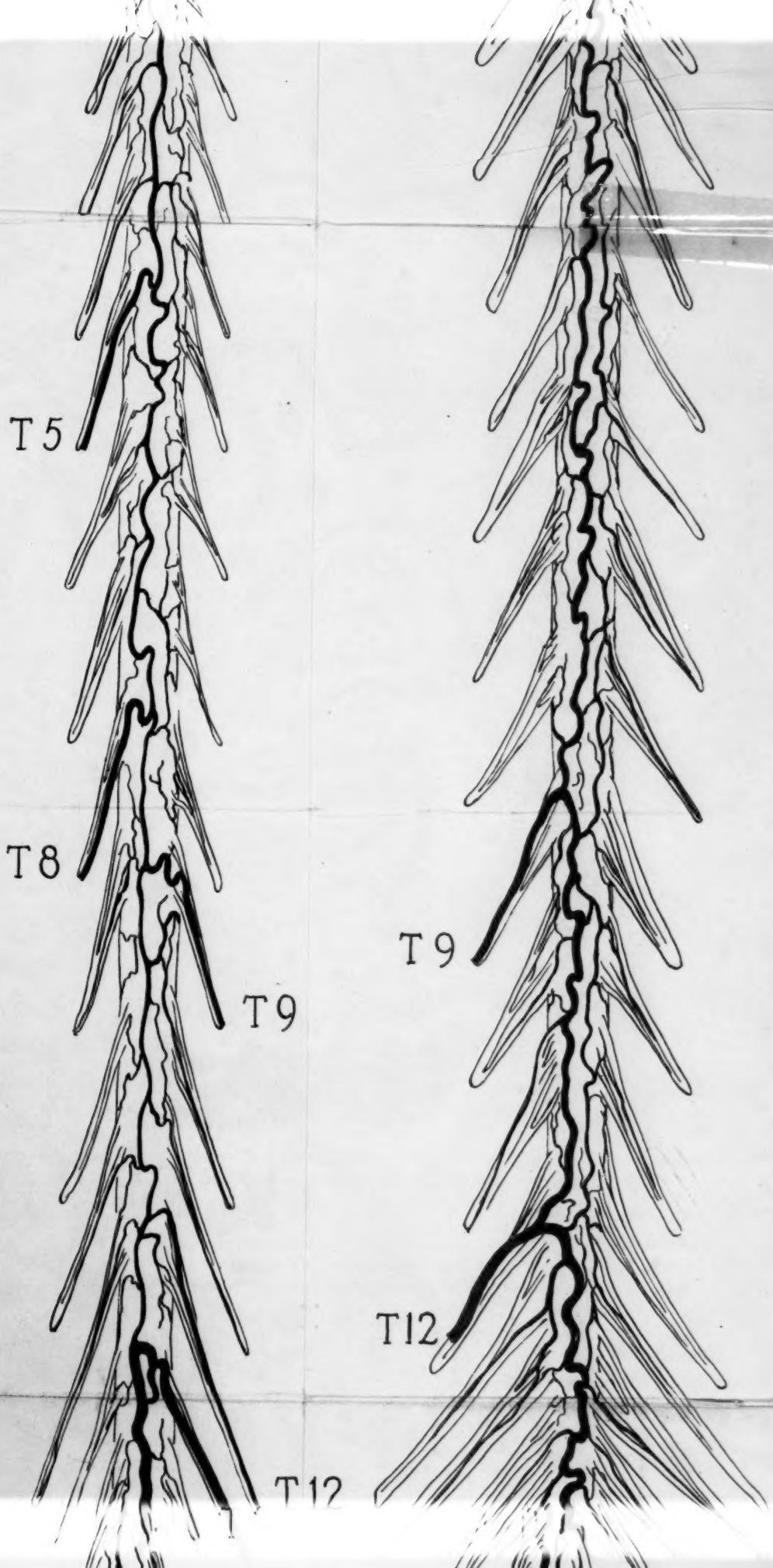
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T12
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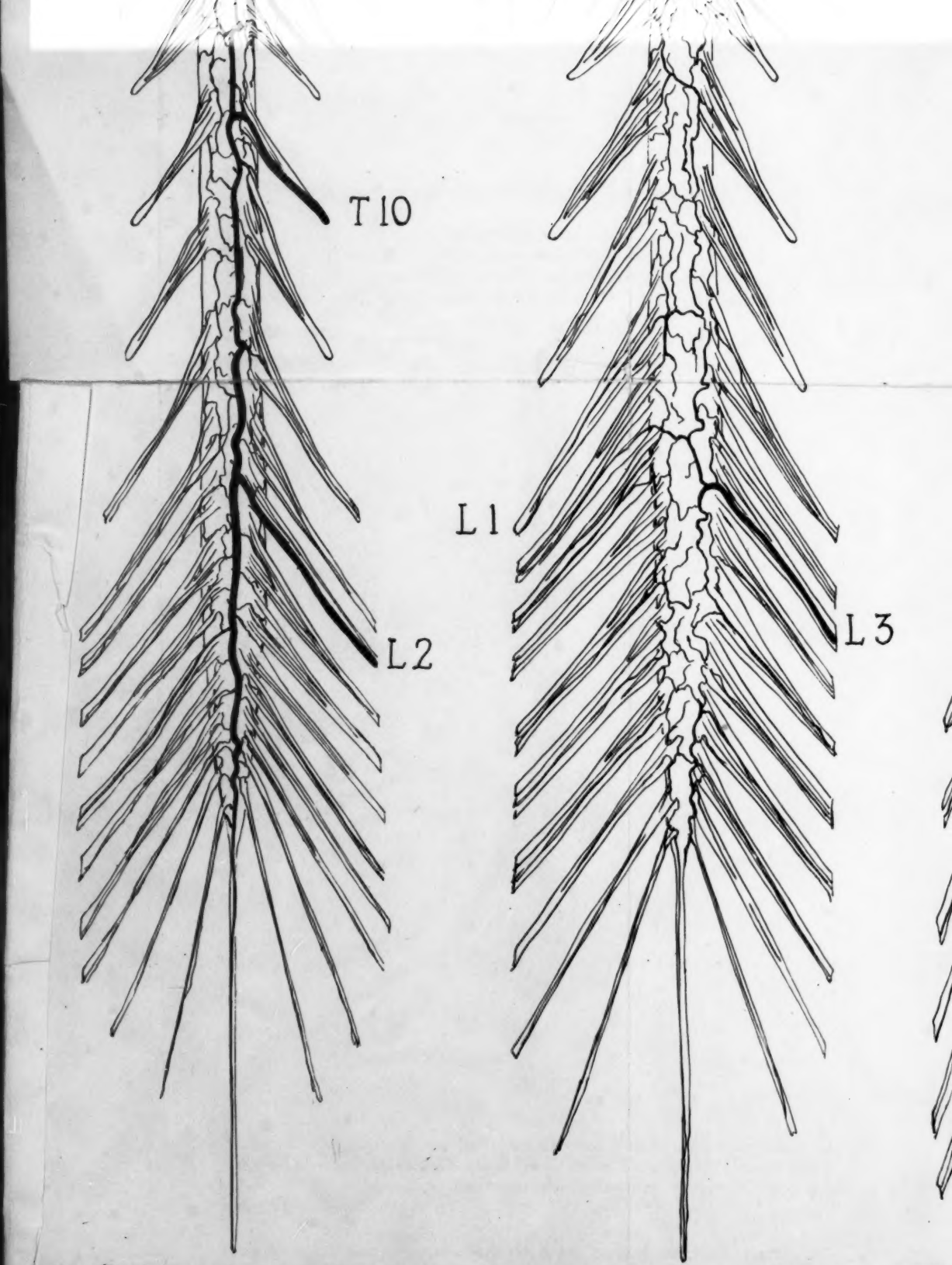
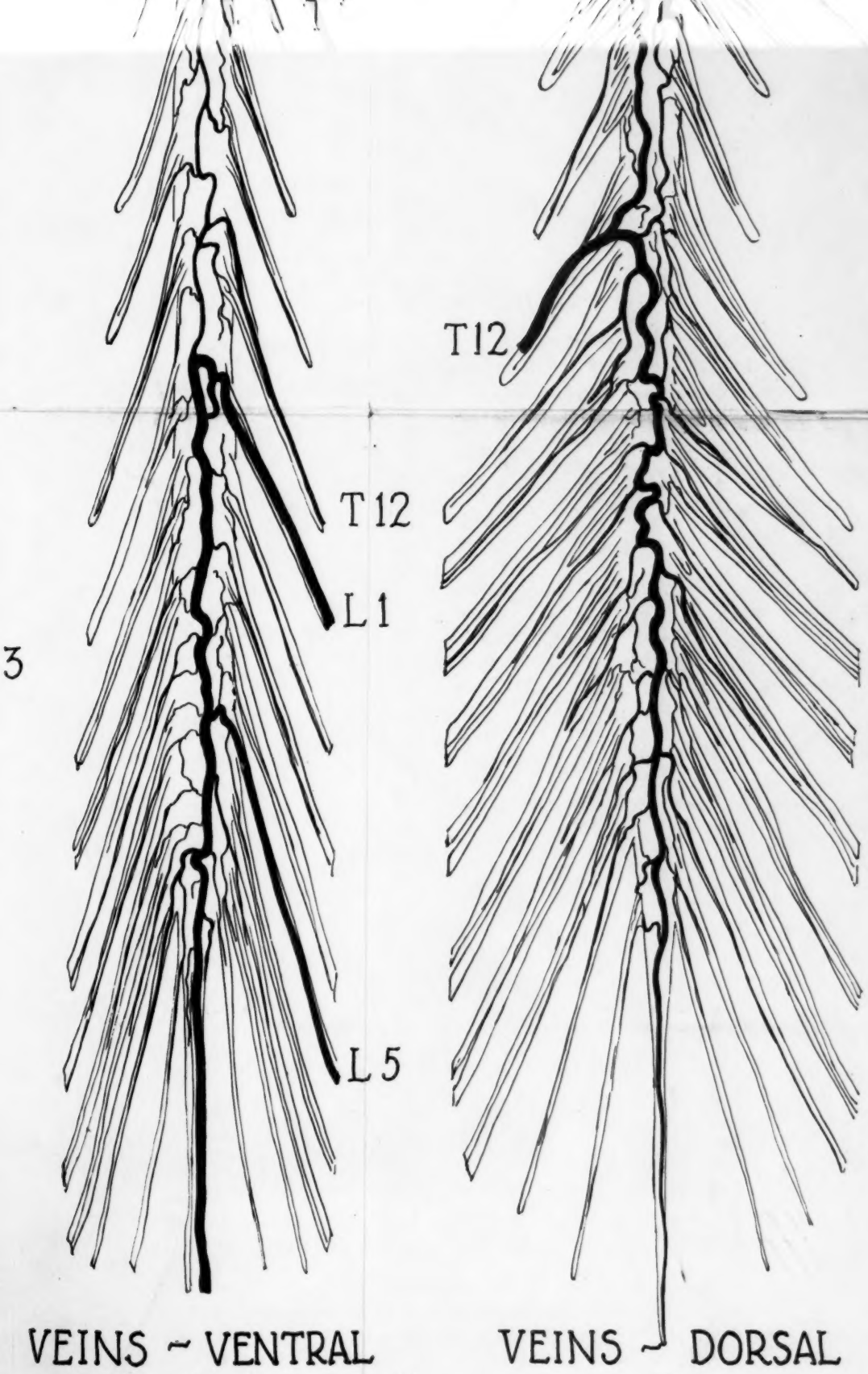



6-A 6-B

Fig. 6.—Diagrams of vessels of the human spinal cord drawn to scale (natural size), on the basis o carrying significant radicular vessels are labeled. In order to facilitate comparison with Kadyi's data, grams. *A*, arteries of the anterior surface of the spinal cord of a man. *B*, arteries of the posterior surfa terior surface.




6-C 6-D

the basis of computation of data, including measurements of diameter, in 26 cases. The roots
lyi's data, the arrangement of the spinal cord and the roots is similar to that in Kadyi's dia-
erior surface of the human spinal cord. *C*, veins of the anterior surface. *D*, veins of the pos-

trunk, measuring 340 microns in the adult and 272 microns in the newborn (table 2). Another set of variations in the width of the truncus arteriosus anterior is of special interest. At any given level, that part of the truncus arteriosus

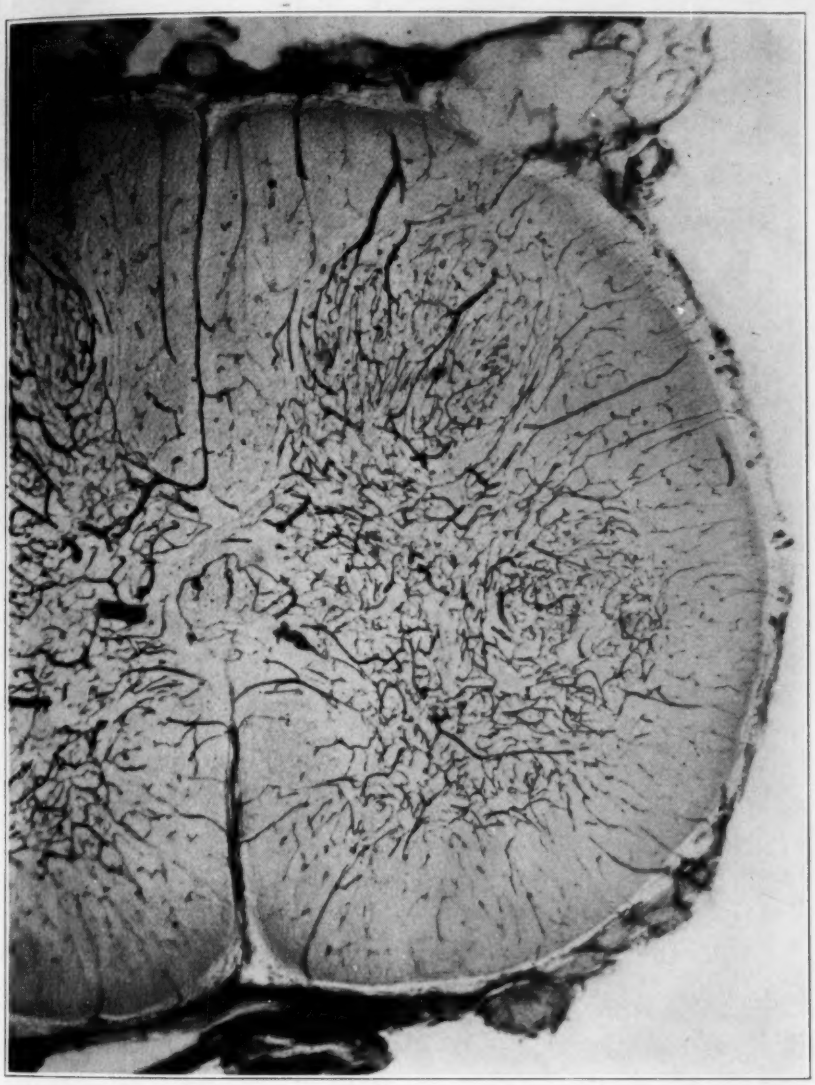


Fig. 7.—Photomicrograph of a cross section of the second sacral segment of the spinal cord of a normal man after injection through the anterior arterial trunk. Enlargement, 23 ×.

anterior is relatively the narrowest which is halfway between two adjoining significant radicular arteries, as though the region equidistant from large radicular branches were the watershed between the two adjoining districts of irrigation.

This is especially striking in the middle thoracic region, where the distance between significant radicular branches is longest, for instance, at the eighth thoracic segment, shown in figure 6 *A*, which is halfway between one significant right radicular artery, at the fifth thoracic segment, and another significant left radicular artery, at the tenth thoracic segment. It is obvious, therefore, that the blood which replen-

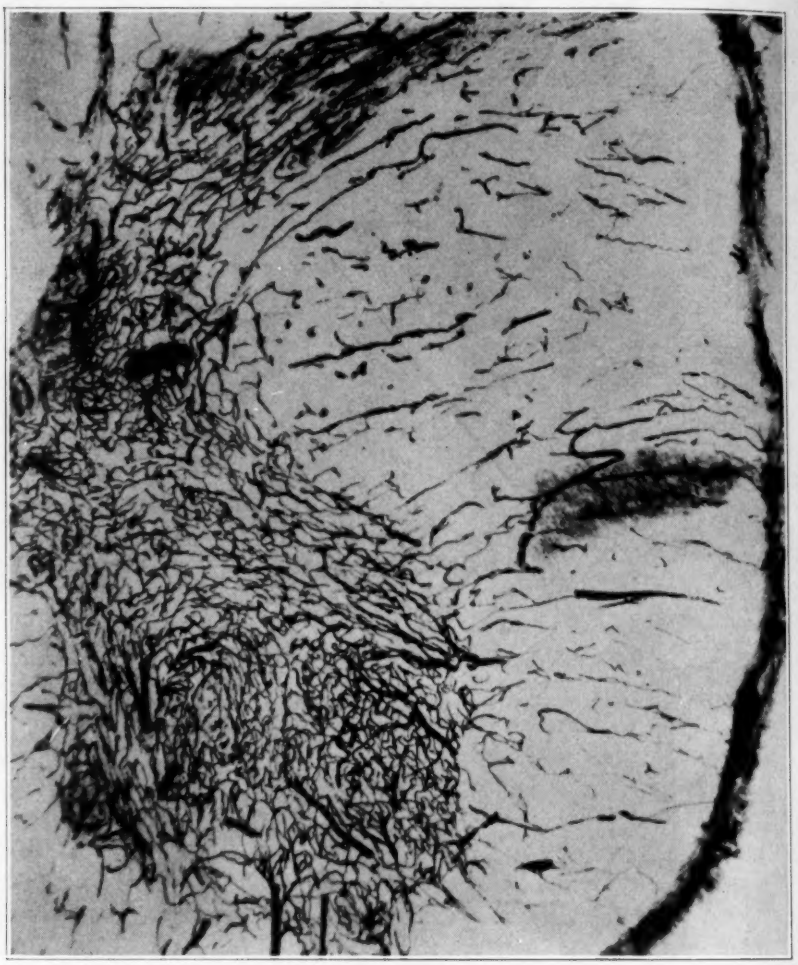


Fig. 8.—Photomicrograph of a cross section of the fourth lumbar segment of the spinal cord of a normal man. Benzidine stain; enlargement, 26 ×.

ishes the truncus arteriosus anterior at this point of the middle thoracic region, the blood supply on which this portion of the cord depends, comes from segmental levels above (for instance, the fifth thoracic) and below (for instance, the tenth thoracic). It is no idle speculation to assume that the lower middle thoracic region owes its early vulnerability in pernicious anemia to this anatomic peculiarity, namely, to being placed at the end of a long side road of the circulation.

This suggestive evidence that the flow of blood in the truncus arteriosus anterior from two major radicular arteries may be in opposing (converging) direc-

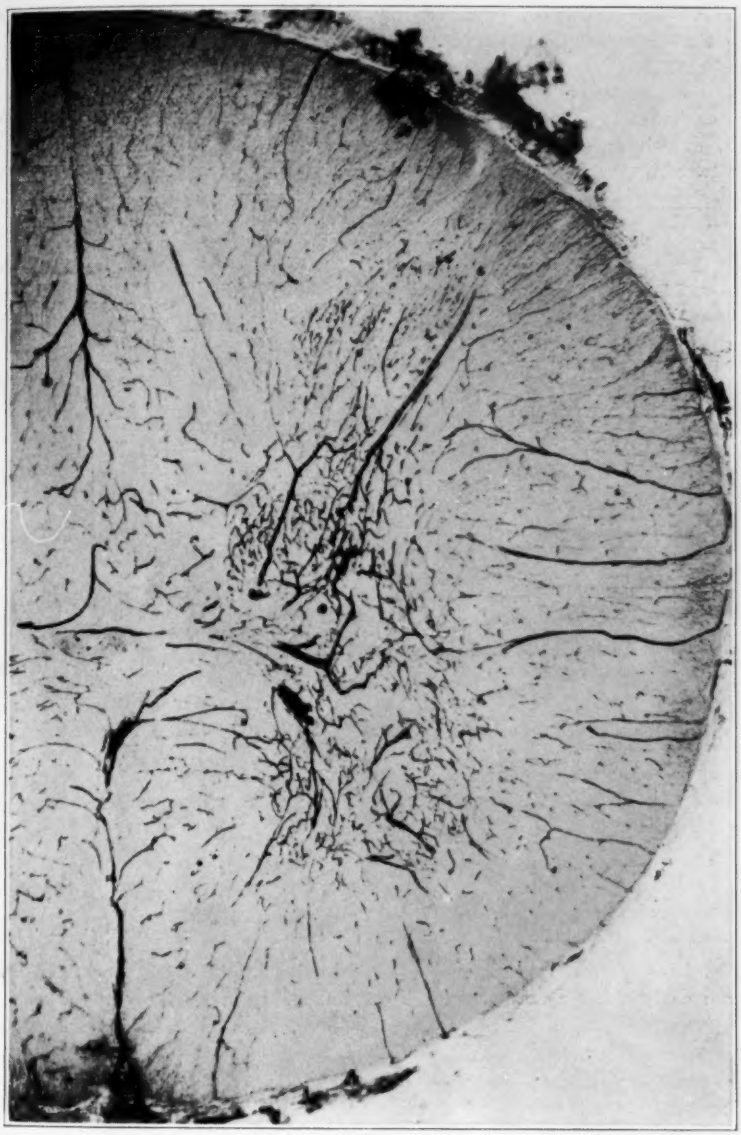


Fig. 9.—Photomicrograph of a cross section of the first lumbar segment of the spinal cord of a normal man, after injection through the anterior arterial trunk. Enlargement, 19 ×.

tions (first suggested by Adamkiewicz) is also supported by the experiences obtained in performing the injections. The anastomoses between the lower cervical and the upper thoracic region are frequently so thin and inadequate that from above injections can be made only into the cervical region and from below only into the lumbar and the thoracic region.

The posterior radicular arteries (fig. 6*B*) are similar in distribution. The anastomoses, however, are accomplished by two somewhat irregular and incomplete chains located lateral to the midline, close to the dorsal edge of the posterior roots, though in some places one or the other branch may run closer to the midline. All posterior radicular arteries and their anastomoses are smaller than

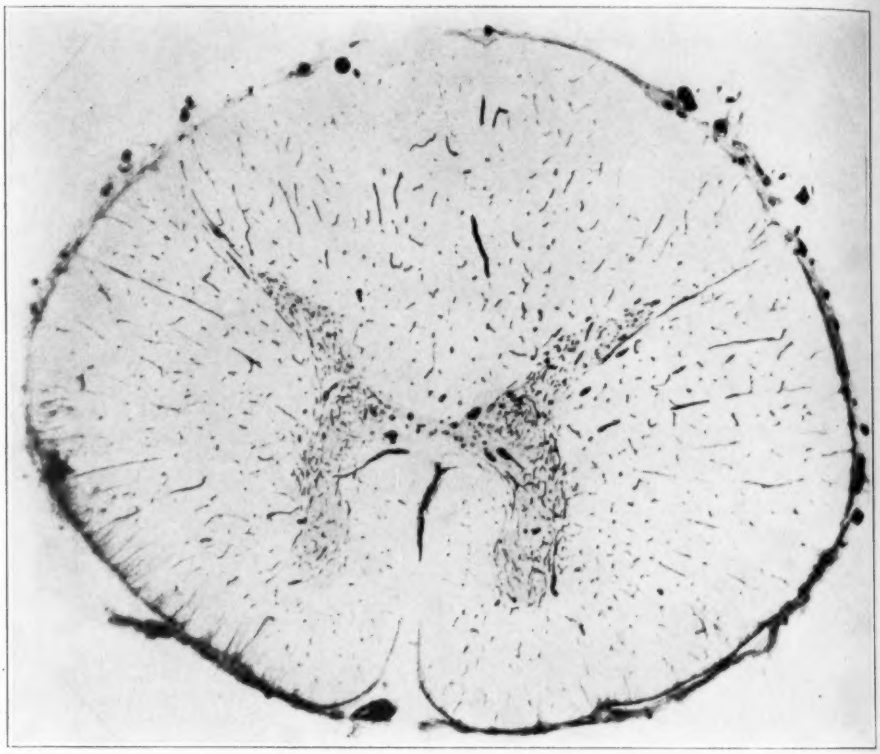


Fig. 10.—Photomicrograph of the cross section of the ninth thoracic segment of the spinal cord of a normal man. Benzidine stain; enlargement, 14 ×.

the anterior radicular arteries and their anastomoses. There is no continuous posterior spinal artery.

The anterior radicular veins of the sixth order (fig. 6*C*) essentially resemble in distribution the anterior radicular arteries. There are from six to eleven significant veins which are distributed in nonsymmetric arrangement and usually do not approach the spinal cord by the same roots as the significant radicular arteries, though they may coincide occasionally. There is one vena radicularis magna between the twelfth thoracic and the third lumbar segment, most frequently on the left. The significant radicular veins in the cervical region are usually seen at the third, fourth and fifth segments; there is one in the upper thoracic

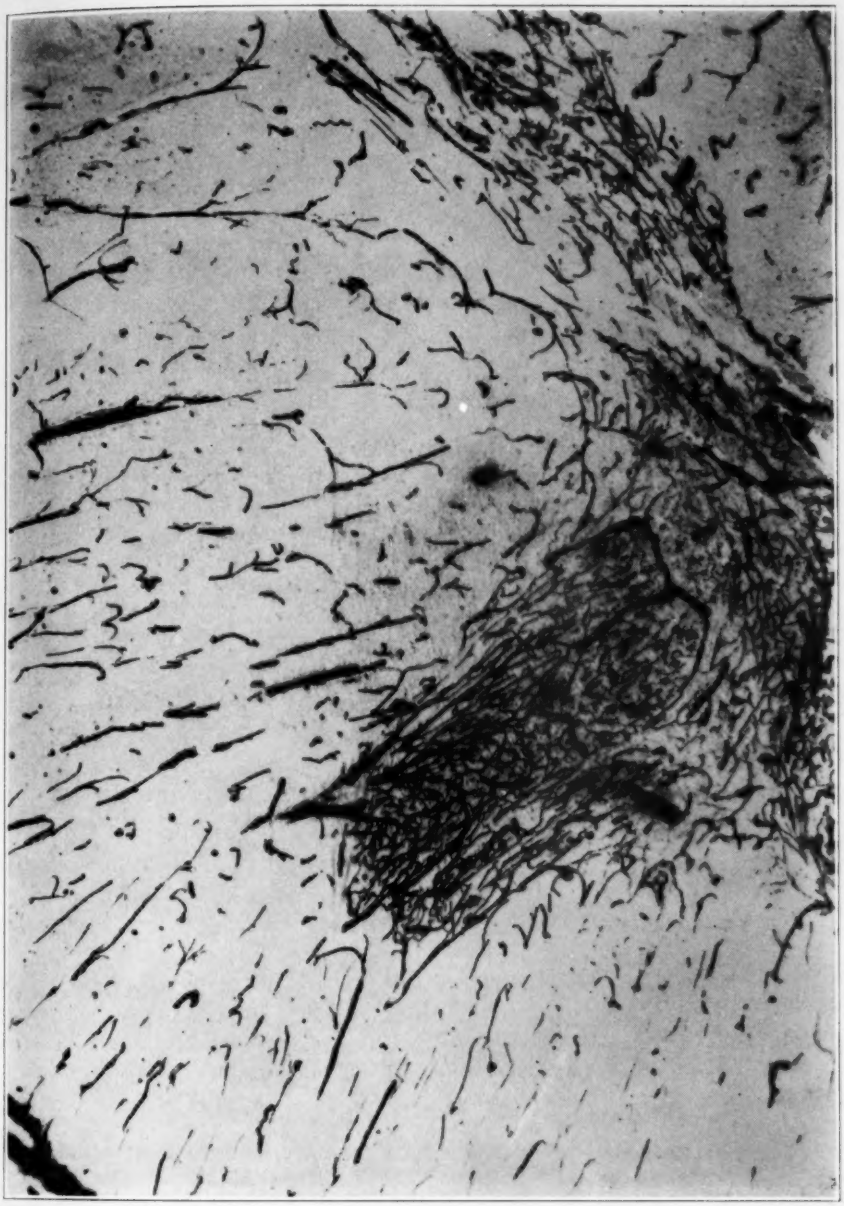


Fig. 11.—Photomicrograph of a cross section of the sixth cervical segment of the spinal cord of a normal man. Benzidine stain; enlargement, 26 ×.

region at the first segment and in the middle thoracic region at the fifth or sixth segment; in the lower thoracic region one or two are seen between the seventh and the ninth segment, and one, though smaller, may be observed at the twelfth segment. There is an anterior chain of anastomoses, the truncus venosus anterior, in the midline closely lateral and dorsal to the truncus arteriosus anterior, so that on inspection from the ventral surface the venous trunk is partly covered by the arterial trunk. At any given level, that part of the truncus venosus anterior is

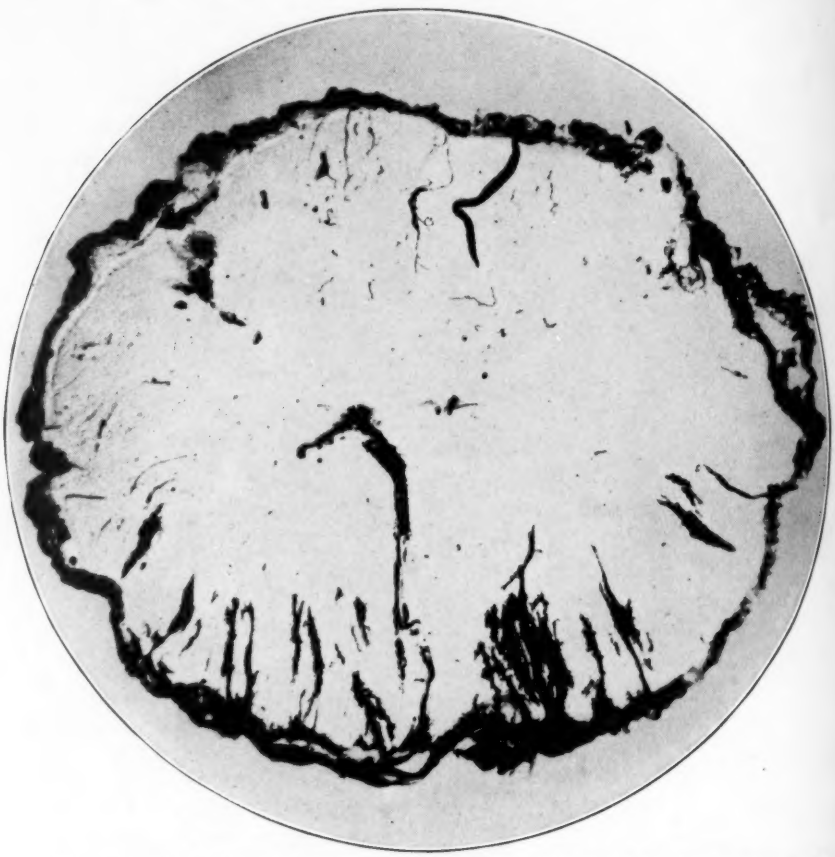


Fig. 12.—Photomicrograph of a cross section of the third lumbar segment of the spinal cord of a normal man, after injection through the anterior venous trunk. Enlargement, 13 ×.

relatively the narrowest which is at about the border between the upper and the middle third of the distance between two adjoining large radicular veins, as though this region were the watershed between two adjoining larger districts of venous drainage. One gains the impression that the large radicular vein usually seen at the fifth or sixth thoracic segment is draining all the segments from the second to the sixth or seventh thoracic segment and that the large radicular veins at the eighth and ninth thoracic levels are draining from the seventh to the eleventh segment.

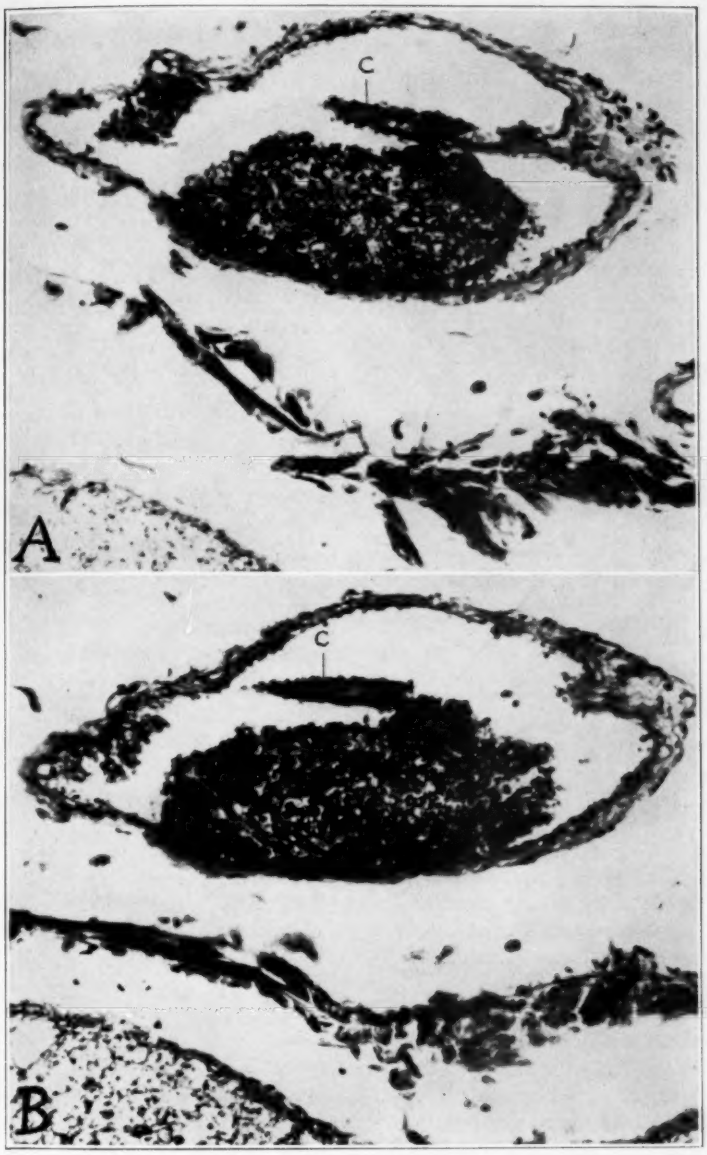



Fig. 13.—Photomicrograph showing a meningeal vein of the fifth order close to a bifurcation, from the spinal cord of a normal man. The width of the vein is 180 microns. *A* and *B* are serial sections from the same series, taken five sections (50 microns) apart. Here, *c* indicates a rudder-like prolongation of the wall at the inner angle of bifurcation, 230 microns in length, presumably serving as the cusp of a monocuspid valve. Compare with the diagram in figure 14. Note the accidental accumulation of blood (post mortem) on one side of the valve. Masson's trichrome stain; enlargement, about 142 ×.

The posterior radicular veins (fig. 6 *D*) are similar in distribution to the posterior radicular arteries. They are, however, united by one median anastomotic chain, the truncus venosus posterior, which is always larger than the truncus venosus anterior.

Kadyi's observations were similar; study of his colored plates is recommended to any one interested in the subject.

This differentiation of the radicular arteries from the primitive segmental pattern, which is well preserved in the rabbit, is as well pronounced in the cat as in man; in a recent injected specimen from a cat we observed the arteria radicularis anterior magna at the third lumbar segment on the left and the vena radicularis anterior magna at the second lumbar segment on the right; there were four significant cervical radicular arteries, and one each in the upper, middle and lower thoracic regions.

As to the arteries of the anterior sulcus (sulcal arteries) and their continuations, the paracentral arteries (figs. 1, 2 and 3), we can fully confirm Kadyi's obser-

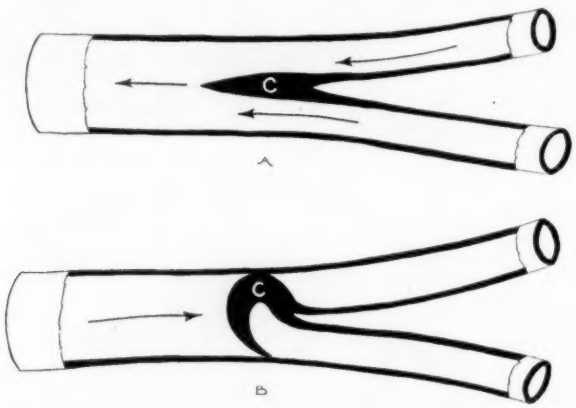



Fig. 14.—Diagram of the presumable function of a monocuspid valve of a spinal vein. *A* indicates position of the valve during normal flow of blood; *B*, the valve in action during regurgitation of blood, and *C*, a rudder-like prolongation of the wall of the vein at the inner angle of bifurcation, presumably serving as the cusp of a monocuspid valve.

vations already cited. This fact guarantees a high degree of independence of the arterial circulation in the two halves of the spinal cord.

By injection of the anterior arterial trunk, the intramedullary vessels, including the capillaries and veins, can be well filled. The well known fact of the greater capillary density of the gray matter than of the white matter need not be emphasized (figs. 7 to 11). The arrangement of the capillaries and precapillaries of the anterior horns in groups corresponding to groups of ganglion cells, as emphasized by Djorup,[7] is well shown in figures 8 and 11. The intramedullary vessels of the larger orders, especially those of the fourth and third orders, show an interesting difference in the various levels of the cord. In cross sections through the sacral and lumbar regions, many of the vessels, especially in the white matter,

7. Djorup, F.: Ganglieceller og arterier: I. Cervikalpartiet af menneskets rygmarv (with an English résumé), Copenhagen, Denmark, Host, 1923, p. 108.

are cut longitudinally (figs. 7, 8 and 9), while in the thoracic region, especially at its lower middle level, most of them appear as short oblique or cross sections (fig. 10). In the cervical region the slant of the vessels is halfway between the predominantly transverse seen in the lumbar region and the predominantly longitudinal seen in the thoracic region. This observation tends to corroborate our conclusion drawn from the arrangement of the vessels of the sixth order that the blood supply of the middle thoracic region of the cord comes from segmental levels above and below. Purely segmental circulation is well developed in the sacral and lumbar regions and less well established in the cervical portion, while it is only rudimentary and is largely replaced by a transsegmental circulation in the thoracic region, especially in its lower middle portion.

By injection of the truncus venosus anterior, the intramedullary veins of the fourth order and a few of the third order, i. e., the paracentral vein and all the large veins of the periphery of the white matter, are well filled (fig. 12), but injections of the small veins of the second order and the capillary network could not be made from the large venous channels. This finding suggests the existence of valves at the point of transition from the veins of the fourth order to those of the third. In our attempts to demonstrate the valves in thin serial sections, we found that no bicuspid valves exist but that at the points of division of veins the inner angle of the bifurcation is prolonged by a rudder-like attachment which protrudes back into the lumen of the large mother vein (figs. 13 and 14 *A*). The length of this rudder exceeds the diameter of the vessel, the relation being approximately 23 : 18, and it is conceivable that the structure may function like the cusp of a monocuspid valve (fig. 14 *B*). We have seen morphologic pictures suggesting such a function in veins of the fifth order, as well as at the points of subdivision between veins of the fourth and those of the third order.

## COMMENT

The observation which we wish to emphasize is the striking difference in size between the various radicular arteries and veins in the spinal cord. The blood supply of the spinal cord depends on from six to eight anterior radicular arteries, from five to eight posterior radicular arteries, from six to eleven anterior radicular veins and from five to ten posterior radicular veins, the largest always being an artery and vein in the lumbar region, the arteria and the vena radicularis magna. This fact is of interest both to the neurosurgeon and to the neuropathologist. Occasional instances in which surgical section of a root was followed by myelomalacia appear to us to have been due to the fact that one of the roots carrying an important vessel had been sectioned. To the neuropathologist, our observations explain the extension of certain myelomalacias far beyond the site of the vascular occlusion. In a recent observation in a series studied by Herren and one of us (L. A.),[8] thrombosis of the sixth thoracic anterior radicular vein and of the adjacent part of the truncus venosus anterior corresponding to the sixth thoracic segment, due to compression of the radicular vein by a tumor metastasis in the

8. Alexander, L., and Herren, Y.: Compression Myelitis Due to Extramedullary Tumors and Its Relation to the Vascular System of the Spinal Cord, to be published.

intervertebral foramen, had caused myelomalacia involving symmetric anterolateral parts of the cord and extending from the seventh to the second thoracic segment. There had been no direct compression of the cord or narrowing of the spinal canal by the tumor.

Our observations, as well as those previously made by Tanon,[3] tend to indicate that the lumbar radicular vessels are an important source of blood supply for the major part of the spinal cord. The middle thoracic section of the spinal cord has the poorest local segmental circulation. This may be of importance in a great many conditions, apart from obvious anoxia from vascular occlusion, such as subacute combined degeneration of the cord occurring in pernicious anemia, a condition in which damage occurs first in the middle thoracic region. Myelitic processes of various types are most frequent in this region. Adamkiewicz [2] made a similar correlation.

The fact that by arterial injection the entire vascular system (arteries, capillaries and veins, figs. 7 and 9) can be filled, while by venous injection, except for the paracentral veins of the fourth order and one or another of their branches of the third order, only large and middle-sized venules of the fourth and the third order in the white matter of the spinal cord can be filled (fig. 12) is of special interest in view of Putnam's recent investigations. Putnam [9] observed that after experimental occlusion of meningeal veins the resulting lesions involved the white matter selectively, resembling those of disseminated leukoencephalitis or of multiple sclerosis. It is obvious from our injection preparations that occlusion of venules of the fifth order at the meningeal surface of the spinal cord leads to congestion and stasis in the venules of the fourth and third orders in the underlying white matter only, causing damage to the adjacent parenchyma (probably streaklike or plaquelike demyelinations), while the subjacent gray matter is not only protected from venous backflow by the valvelike structures which we have described but, in addition, because of its richer collateral circulation, finds an outlet for its venous blood through other channels, notably the paracentral veins. The only veins occlusion of which causes destruction of the anterior part of the gray matter of the spinal cord as well as of the white matter are the paracentral veins. Our observations regarding the normal anatomic pattern of the spinal venous system provide a striking confirmation of Putnam's [10] pathogenetic conclusions.

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9. Putnam, T. J.: Studies in Multiple Sclerosis: IV. "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, Arch. Neurol. & Psychiat. **33**:929-940 (May) 1935.

10. Putnam, T. J.: Lesions of "Encephalomyelitis" and Multiple Sclerosis: Venous Thrombosis as the Primary Alteration, J. A. M. A. **108**:1477-1480 (May 1) 1937.

SUMMARY

1. The blood supply of the human spinal cord depends on from six to eight anterior radicular arteries, from five to eight posterior radicular arteries, from six to eleven anterior radicular veins and from five to ten posterior radicular veins, the largest always being an artery and vein in the lumbar region, the arteria and the vena radicularis magna.

2. The physiologic, clinical and pathologic significance of this observation is discussed with reference to its surgical implications.

3. The intramedullary vessels are classified according to order of magnitude.

4. The plane of distribution of larger intramedullary vessels is predominantly transversal in the sacral and lumbar regions and predominantly longitudinal in the thoracic region, while the slant of the vessels in the cervical region is halfway between the two.

5. While by injection from the large arteries the intramedullary arterial system, the capillary network and the venous system can be filled easily, by injection from the large veins filling only of the large intramedullary venules of the fourth order is complete and that of veins of the third order is incomplete. The venules of the second order, the capillary network and the arterial system cannot be reached by venous injection, presumably owing to the presence of valves. The morphologic characteristics of these peculiar monocuspid valvelike structures are described.

# SULCAL AND INTRINSIC BLOOD VESSELS OF HUMAN SPINAL CORD

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AND
LEO ALEXANDER, M.D.
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The agreement which clinicians have recently reached regarding the diagnosis of vascular disturbances of the cord, especially of the anterior spinal artery, is paradoxically not reflected in their accounts of the vascular anatomic relations of the cord. The authors of popular textbooks of neuropathology [1] and those [2] of papers in which cases of disease of the anterior spinal artery are reported have differed almost to a man in their conception of the underlying anatomic structure.

In this issue Suh and Alexander [3] give a comprehensive account of the surface vascular anatomic pattern of the spinal cord and an implication of the damage which may be expected in pathologic conditions of the several major vessels mentioned.

The present paper concerns itself with the intrinsic vascular anatomic relations of the human spinal cord in an effort to introduce unity into the ideas concerned particularly with the branches of the so-called anterior spinal artery and anterior spinal vein.

## MATERIAL AND METHODS

The material was obtained at over 30 postmortem examinations made as a routine at the Boston City Hospital. In none of these cases was there disease of the spinal cord. The spinal cords were removed *in toto,* and various substances

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From the Department of Neurology, Harvard University Medical School, and the Neurological Unit, the Boston City Hospital.

1. Buzzard, E. F., and Greenfield, J. G.: Pathology of the Nervous System, London, Constable & Company, 1921. Cobb, S.: The Cerebrospinal Blood Vessels, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 2, pp. 575-610.

2. Grinker, R. R., and Guy, C. C.: Sprain of Cervical Spine Causing Thrombosis of the Anterior Spinal Artery, J. A. M. A. **88**:1140 (April 9) 1927. Schaller, W. F.; Roberts, A. M., and Stadtherr, E. F.: Acute Myelitis (Myelomalacia): Syndrome of Occlusion of the Anterior Spinal Artery at the Fifth Cervical Cord Segment, ibid. **99**:1572 (Nov. 5) 1932. Tauber, E. S., and Langworthy, O. R.: A Study of Syringomyelia and the Formation of Cavities in the Spinal Cord, J. Nerv. & Ment. Dis. **81**:245, 1935.

3. Suh, T. H., and Alexander, L.: Vascular System of the Human Spinal Cord, Arch. Neurol. & Psychiat., this issue, p. 659.

were injected into the anterior spinal artery in the lumbar region, the most suitable of which was a mixture of 1 part of india ink to 3 parts of solution of formaldehyde U. S. P. (1:10). In many instances differential injections into the anterior spinal artery and the vein were made, and in a few instances injections were made into the larger dorsal radicular arteries alone. The material was then fixed in formaldehyde *in toto* and subsequently treated in several ways. In some instances, the lateral columns were removed from representative sections of the various levels; in others, cross sections or sagittal sections were made of the various levels, and in a larger number of cases the anterior septum and the adjacent part of the central gray matter were separated from the rest of the cord by anatomic dissection. All material, however prepared, was made transparent in Spalteholz' solution after his method. When cleared, the material, immersed in Spalte-


Fig. 1.—Photomicrograph (Lepehne-Pickworth stain; × 6) of a longitudinal diagonal section of the cervical portion of the spinal cord in man. At the top of the section is the regular vascular bed of the posterior gray column, and at the bottom, the irregular vascular bed of the anterior gray column. The variations in the depth of the vascular bed correspond with the beaded nature of the nuclear masses of the anterior gray column.

holz' solution, was examined with the aid of a binocular dissection microscope. The course and branching of vessels in thick sections were thus easily followed. In some other cases noninjected material was stained with benzidine (Doherty, Suh and Alexander[4]).

4. Doherty, M. M.; Suh, T. H., and Alexander, L.: New Modifications of the Benzidine Stain for Study of the Vascular Pattern of the Central Nervous System, Arch. Neurol. & Psychiat. **40**:158 (July) 1938.

## RESULTS

That the vascularity of the gray matter is greater than that of the white matter of the spinal cord has long been common knowledge. Similarly, it is well known that the bulk of anterior gray substance is not uniform but is arranged as a string of beads, each bead comprising a segmental nuclear mass (Djorup[5]). This beaded arrangement of the anterior gray substance does not hold true for the posterior gray column. Here the arrangement is one of a solid column, varying somewhat in thickness at different levels. Figure 1 shows the vascular arrangements in the two gray columns of the cord. There are a constant depth of vascular bed in the posterior gray column and a series of bulbous arborizations within the nuclear beads in the anterior gray column.

The anterior spinal artery receives several anterior segmental arteries of irregular size.[3] It is by means of these irregularly sized arteries that most of the

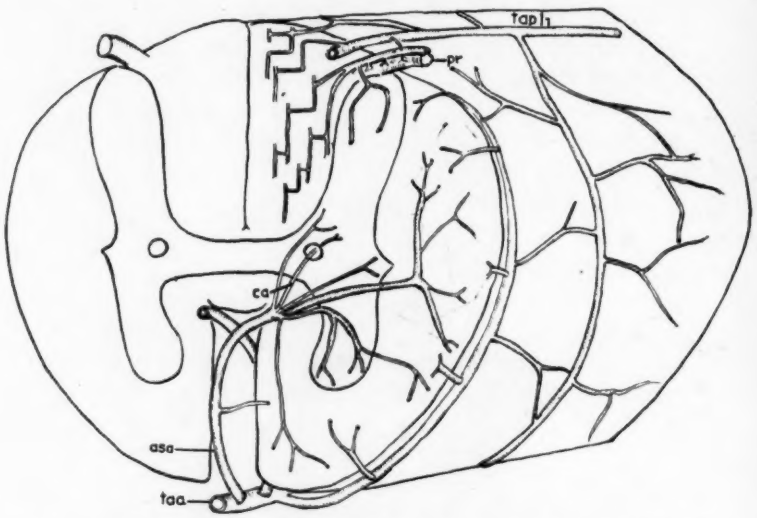


Fig. 2.—Diagrammatic drawing of the arteries and their distribution in the spinal cord. Only branches of from the sixth to the third order are included. Of these, *asa* indicates the anterior sulcal artery; *ca*, the paracentral artery; *tapl*, the posterolateral arterial trunk; *pr*, the posterior root, and *taa*, the truncus arteriosus anterior.

arterial supply of the cord is effected. The branches of the anterior spinal artery, the sulcal arteries, pass upward in the reflection of connective tissue lying in the anterior sulcus and have several characteristics for the various levels of the cord. One fact, however, stands out for all levels, namely, that each anterior sulcal artery contributes to the arterial supply of only one side of the spinal cord, either the right or the left (fig. 2).

The lumbosacral region receives the richest blood supply (fig. 3 *A* and *B*). At this level the sulcal arteries leave the anterior spinal artery at right angles

5. Djorup, P.: Ganglieceller og arterier: I. Cervikalpartiet af menneskets rygmarv, Copenhagen, Host, 1923, p. 108.

and pass upward in the septum, giving off infrequent branches to the septo-marginal white fibers. In the depth of the sulcus the artery turns laterally either to the right or to the left, under the anterior white commissure, and pierces the substance of the cord (fig. 2). The vessel then divides, sending one branch in the paramedian vascular canal to anastomose with higher and lower levels, another to supply the gray commissure and Clarke's dorsal column, others to the

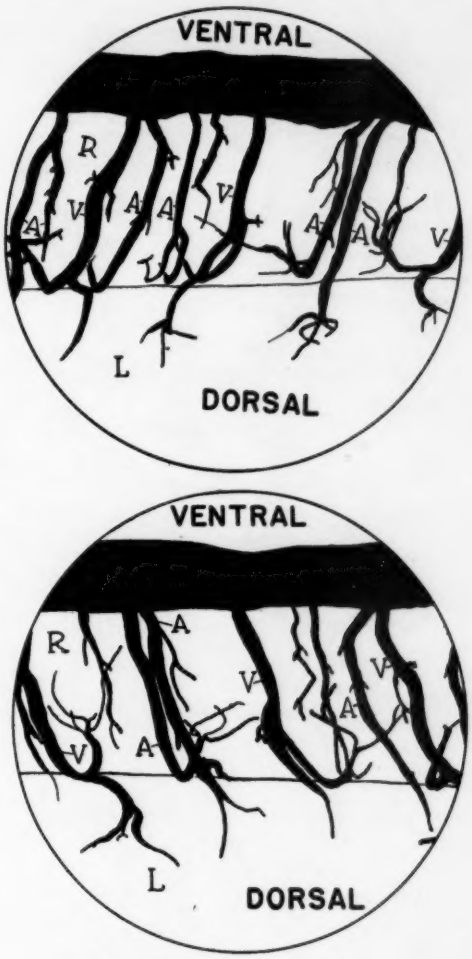


Fig. 3.—Retouched photomicrographs (about × 10) of the injected sulcal arteries and veins of the lumbar portion of the human spinal cord. In this figure and in figures 4 and 5, *R* indicates the right side; *L*, the left side; *A*, an artery, and *V*, a vein. The thin approximately horizontal line is the point of attachment of the connective tissue septum in the depth of the anterior median sulcus. Spalteholz preparations; sagittal view.

several nuclei in the anterior and lateral gray horns and still others to the white matter of the anterior and lateral funiculi. We wish to emphasize especially

that the lateral pyramidal tract is nourished by branches of the anterior spinal artery.

Only in the lumbosacral region, and here only occasionally, is a sulcal artery seen to divide into two sulcal branches from a short common trunk. In our preparations we have not observed that these occasional branches supply more than the same side of the cord. The sulcal arteries for either side are not regularly alternating.

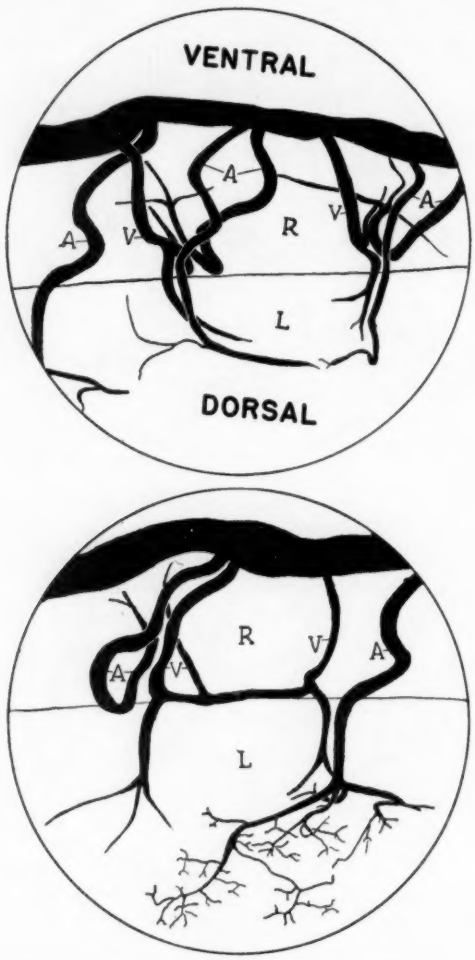


Fig. 4.—Retouched photomicrographs (about × 10) of the injected sulcal arteries and veins of the cervical portion of the human spinal cord. Spalteholz preparations; sagittal view.

The next most abundant blood supply is in the cervical region (fig. 4 *A* and *B*). Here the sulcal arteries leave the anterior spinal artery in a slightly oblique course, and it is here that there is the greatest regularity in vessels supplying the alternate sides of the cord. At this level, rather constantly, there appeared

to be two arteries on each side, that is, four sulcal arteries altogether, for each segment. The distribution of these vessels is like that in the lumbar region, the only differences being due to absence of such structures as the lateral gray horn.

The thoracic region has the poorest blood supply (fig. 5); viewed from this standpoint it appears to be the most vulnerable. The sulcal arteries here leave the anterior spinal artery with considerable obliquity and run dorsad and craniad in the septum. There is considerable irregularity in the alternate supply to either side, and occasional areas are seen where one sulcal artery alone supplies one side only for a whole segment. To compensate for this dearth, there are a substantial number of descending and ascending intraspinal arterial branches. One such vessel was traced for a distance of four segments. The intraspinal distribution of the sulcal artery is similar in every other way to that in the lumbar and cervical segments.

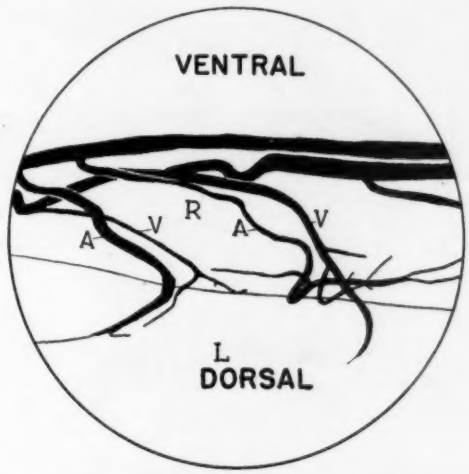


Fig. 5.—Retouched photomicrograph (approximately × 10) of the injected sulcal arteries and veins of the thoracic portion of the human spinal cord. Spalteholz preparation; sagittal view.

The characteristics and course of the anterior spinal vein have been described by Suh and Alexander.[3] It lies directly in the middle of the open sulcus, with the anterior spinal artery anterior and to one side of it. With its distribution similar to, but not quite identical with, that of the anterior spinal arterial trunk, the anterior spinal venous trunk is seen by its distribution and anastomoses to furnish venous drainage roughly to the part of the cord which is in front of a curved line passing through the posterior gray horns and the gray commissure. In a forthcoming report we shall describe a case of thrombosis of the anterior spinal vein in which exactly this circumscribed area was necrotic.

One description of the anterior sulcal veins is sufficient for all levels. Even at the levels where the anterior sulcal arteries leave the anterior spinal artery obliquely, the veins maintain a somewhat more perpendicular course. The sulcal veins do not adhere to the rule for venae comitantes elsewhere in the body. The veins are less frequent than the sulcal arteries, no constant ratio being

observed. They receive many tributaries from the sulcomarginal white matter as they pass upward in the septum and anastomose freely with each other. Almost all the veins, in contrast to the sulcal arteries, bifurcate in the depth of the anterior sulcus, thereby supplying both halves of the cord (figs. 3 to 6). Thus, each anterior sulcal vein usually drains both sides of the spinal cord, while each sulcal artery supplies only one. A few veins, however, also drain only one side.

The venous branches to each side pass laterally under the anterior white commissure and again divide: one branch passing up and down in the paramedian vascular canal and the other branches draining the various medial nuclear groups in the anterior gray horn. Occasionally a relatively large branch is given off from the anastomotic vein traveling in the paramedian vascular canal and passes to the surface to join the large posterolateral vein (figs. 6 and 7). This vein does not receive many sizable tributary branches, and its caliber remains rather

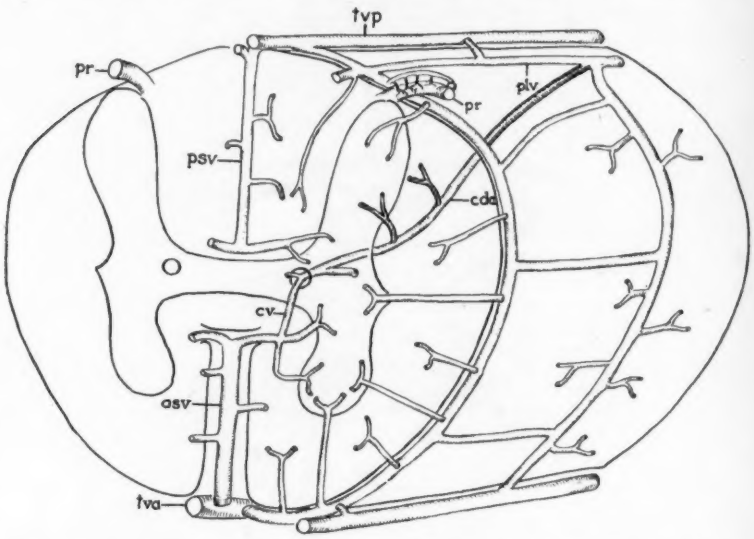


Fig. 6.—Diagrammatic drawing of the veins and their distribution in the spinal cord. Only branches of from the sixth to the third order are included. In this figure, *asv* indicates the anterior sulcal vein; *cda*, the centrodorsolateral anastomosis; *cv*, the paracentral vein; *plv*, the posterolateral venous trunk; *pr*, the posterior root; *psv*, the posterior septal vein; *tva*, the truncus venosus anterior, and *tvp*, the posterior venous trunk.

uniform; this suggests the possibility that this "centrodorsolateral venous anastomosis" serves not so much for return drainage as for the equalization of venous pressure. The venous drainage of the anterior and lateral nuclear groups of the anterior gray horn, the lateral (autonomic) gray horn and the white matter between the point of entrance of the posterior root and the anterior sulcomarginal white bundles is by means of individual veins the course of which is perpendicular to the periphery of the cord in the connective tissue septums. All these vessels join surface veins that anastomose freely with each other and with the anterior and posterolateral spinal veins (fig. 6).

In accordance with the observations of Suh and Alexander,[8] who pointed out that there is no continuous posterior spinal artery and that the large bulk of nourishment to the cord is by way of the anterior spinal artery, injection into the posterior radicular arteries showed distribution of the dye in the posterior gray horn, the posterior white commissure and the posterior funiculus (fig. 2). The posterior radicular artery enters the subarachnoid space with the posterior root and travels with it along the dorsolateral surface of the cord for at least one segment before it dips into the substance of the cord just medial and dorsal to the point of entrance of the posterior root. Along this course this vessel gives off

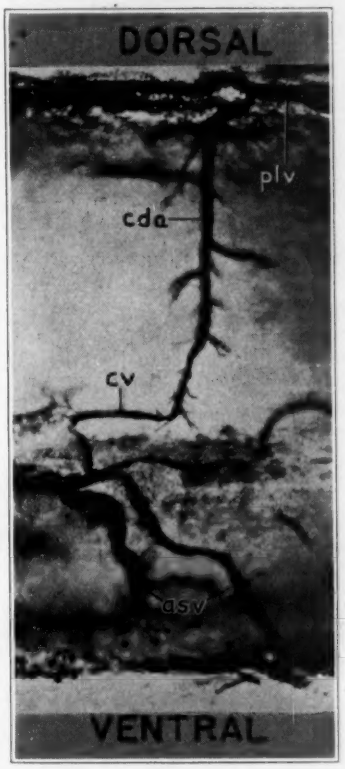


Fig. 7.—Photomicrograph (× 13) of the centrodorsolateral venous anastomosis (*cda*), from a sagittal view of a human spinal cord in which injection was made. The several vessels (*asv*) at the bottom of the photograph are anterior sulcal veins. The anastomotic vessel connects the posterolateral vein (*plv*) at the top of the photograph with the paracentral vein (*cv*).

branches which enter the tiny connective tissue septums and which, by a series of steplike branches, supply the structures named.

The venous drainage of the posterior half of the cord is accomplished in the following manner: The posterior gray horn has a series of fairly regular veins, which arborize around its nuclei and hug them closely; these veins pass to the lateral side of the posterior gray horn to leave the cord just lateral and ventral

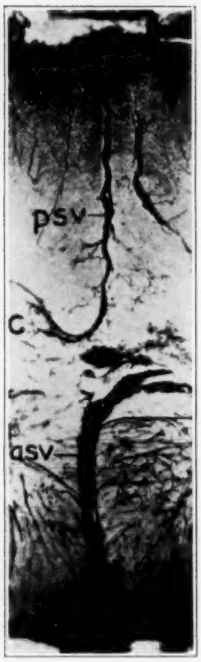


Fig. 8.—Photomicrograph (× 13) of the dorsal septal vein (*psv*) and its branch arborizing around Clarke's column, from a transverse view of the thoracic portion of a human spinal cord in which injection was made. *C* indicates Clarke's column, and *asv*, the anterior sulcal vein.

Fig. 9.—Photomicrograph (× 9.5) of a cross section of the thoracic portion of the human spinal cord in which injection was made through the anterior arterial trunk.

to the point of entrance of the posterior nerve root (fig. 6). As they leave the cord these veins join the large posterolateral veins of the dorsal surface of the cord. These large posterolateral veins also receive short branches from the adjacent white matter which pass outward in the connective tissue septums. The median posterior septum carries a vein of considerable size, which bifurcates in the depth of the septum. In its downward course it receives branches at right angles from the greater bulk of the posterior funiculus. This posterior septal vein bifurcates in the depth of the septum and arborizes about and drains Clarke's column of each side (figs. 6 and 8) and the dorsal white commissure. At the surface the posterior septal veins open into the posterior spinal vein (truncus venosus posterior).

Occasionally, however, Clarke's column may be drained through a posterolateral vein (fig. 9).

## SUMMARY

1. The anterior sulcal arteries supply only one side of the spinal cord at any given level (fig. 2), while most anterior sulcal veins drain both sides (fig. 6). A few sulcal veins, however, drain only one side.

2. The centrodorsolateral venous anastomosis, a wide anastomosing branch between the paracentral vein and one of the large dorsolateral surface veins, is described. In view of the fact that it has comparatively few significant tributaries, it is assumed that one of the functions of this venous anastomosis is to allow a quick exchange between these two large reservoirs of blood for the equalization of venous pressure.

3. The anterior radicular arteries and the anterior spinal arterial trunk supply the anterior horns, the central gray matter, the lateral horns and Clarke's columns and the anterior and lateral tracts, including the anterior and lateral pyramidal tracts.

The posterior radicular arteries and the posterolateral arterial trunks supply the posterior columns and the posterior horns.

4. The anterior spinal venous trunk, by means of the anterior sulcal veins, drains the septomarginal white and the anterocentral gray matter. The same trunk, by means of its transverse meningeal branches and their tributary individual straight intraspinal veins of the fourth order, drains the anterior and anterolateral gray horns, the lateral gray horns and the anterolateral and lateral white matter, including the lateral pyramidal tracts, with the exception, in some places, of a narrow strip of white matter laterally adjacent to the posterior horn (containing a small part of the lateral pyramidal tract), which may be drained both through the anterior and through the posterior venous system by way of the centrodorsolateral venous anastomoses.

The posterior radicular veins and the posterior venous trunk drain the posterior horns, Clarke's columns and the posterior columns and, partly, the narrow strip of white matter laterally adjacent to the posterior horns.

# FOERSTER'S SCHEME OF THE DERMATOMES

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SAN FRANCISCO

According to the painstaking researches of Prof. Otfrid Foerster, of the University of Breslau, Germany, the innervation of the skin by the spinal nerves is not accurately set forth in standard textbooks of neurology. This investigator has had as one of his projects for many years the study of the segmental innervation of the skin. Since the expanded results of his work [1] are not readily available, permission has been granted me to summarize and republish them.

There are several methods of determining the distribution in the skin of the spinal nerves:

1. Dissection. An individual root may be followed by anatomic dissection from a ganglion, through a plexus if necessary, to the ends of the fine branches in the skin.

2. Isolation. Roots above and below that at the level to be investigated may be divided, only the cutaneous representation of the selected root being left to be determined by test.

3. Irritation. Herpes zoster, commonly believed to follow inflammation of ganglia of the posterior roots, produces eruptions in the skin of corresponding areas. Since the process often is limited to a single segment, the distribution of the eruption may be related to definite levels in the spinal cord. Under this heading should come faradic stimulation of the distal remnant of a divided posterior root, by which are produced vasodilatation and consequent demarcation of the affected skin that may be recorded.

4. "Constructive Method." If one sections the tenth, eleventh and twelfth thoracic roots, sensory examination will show the highest level of innervation of the skin by the first lumbar segment. If in another patient one sections the second, third and fourth lumbar roots, one may determine the lower limit of the area of skin innervated by the first lumbar segment. The delineation of the average extent of the single segments by this method is practicable when there is a considerable material at hand.

The laborious method of dissection was employed by Herringham and after him by Bolk. It yielded results that appear to be accurate

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From the Department of Surgery, Stanford University School of Medicine.

1. Foerster, O., in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936.

in regard to shape and position. The dermatomes outlined thus have not, however, the extent that other investigations have shown them to have. The method shows little or no overlap of contiguous segments. There seems little doubt that this is due to the impossibility of following minute filaments to their eventual terminations.

The method of isolation probably is the most dependable of those listed. Before Foerster reported his work with this method the diligent investigations of Sherrington [2] had produced a better understanding of segmental innervation. Sherrington worked with cats and monkeys. From his research came several generalizations applicable to man:

1. The field of each sensory root overlaps those of adjacent roots.
2. Section of a single root does not result in any anesthesia.
3. "Although in the plexuses associated with the innervation of the extremities each segmental nerve contributes sensory fibers to two or more peripheral nerves, the cutaneous distribution of these fibers is not composed of disjointed patches, but forms a continuous field."

Head,[3] through his study of a large number of cases of herpes zoster, gave the most accurate charts of the dermatomes in man before those of Foerster appeared. His work took into account cases of lesions of the cord and cauda equina, as well as the charting of hyperesthetic areas in visceral disease.

In his scheme (fig. 1) little overlap appeared. The question that arose was whether the discrepancies between Sherrington's findings for the monkey and the situation for man were real or depended on the method of study.

The Committee upon Injuries of the Nervous System of the Medical Research Council,[4] in summarizing the experience of the British during the World War with wounds of the spinal cord and cauda equina, published good charts of sensory levels. Apparently it was not possible to determine the exact levels of injury in all cases, and in regard to cervical and thoracic dermatomes the levels arrived at by the British workers and by Foerster disagreed. There was, however, a striking agreement in respect to the configurations of the caudal margins of the dermatomes.

Foerster in attacking the problem used three of the methods mentioned: isolation ("remaining sensibility"), the constructive method

2. Sherrington, C. S.: Experiments in Examination of the Peripheral Distribution of the Fibres of the Posterior Roots of Some Spinal Nerves, Phil. Tr., London, s.B **184**:641, 1894.

3. Head, H., and Campbell, A. W.: The Pathology of Herpes Zoster and Its Bearing on Sensory Localization, Brain **23**:353, 1900.

4. Injuries of the Spinal Cord and Cauda Equina, Reports of the Committee upon Injuries of the Nervous System, Medical Research Council, Special Report Series, no. 88, London, His Majesty's Stationery Office, 1924.

and irritation in the form of faradic stimulation of the posterior roots. Results obtained by stimulation agreed in general with those obtained by the first two methods, but gave smaller areas—areas that correspond to those noted by Head in cases of herpetic eruption. More important conclusions came from isolation and the constructive method.

In caring for a tremendous neurosurgical practice, Foerster had numerous occasions for division of posterior roots. Resulting areas of anesthesia and remaining sensibility were carefully recorded. These

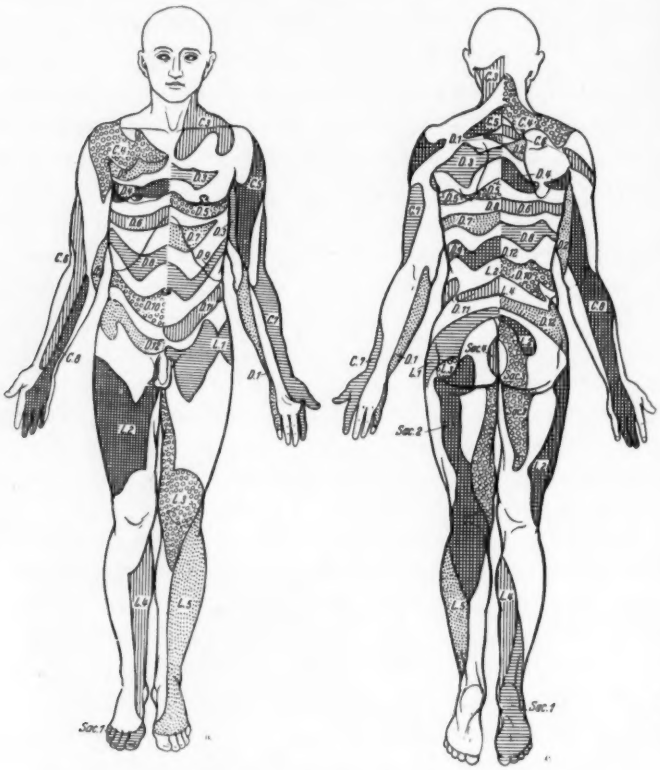

Fig. 1.—The dermatomes in man, according to Head.

records have been presented in more than ninety photographs, which are here summarized in figures 2 to 5. The areas presented are averages; analgesia has been considered to be of major importance, but the boundaries for anesthesia and thermesthesia usually showed slight deviation. The seventh cervical dermatome, which does not appear in the charts, begins lower on the upper part of the arm than the sixth and includes most or all of the hand. The third, the fourth and the fifth sacral dermatome overlap at the anus and about the genitalia.

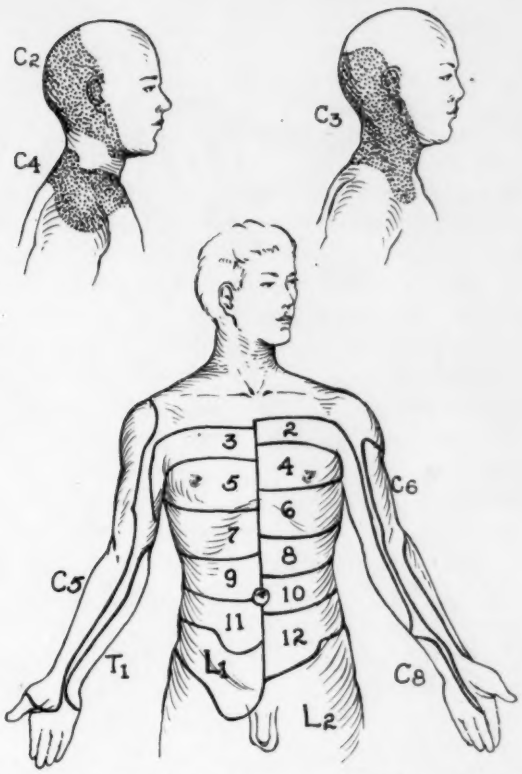


Fig. 2.—Scheme of the cervical and thoracic dermatomes, after Foerster. *C, T* and *L* refer to the cervical, thoracic and lumbar; the numbers indicate segments.

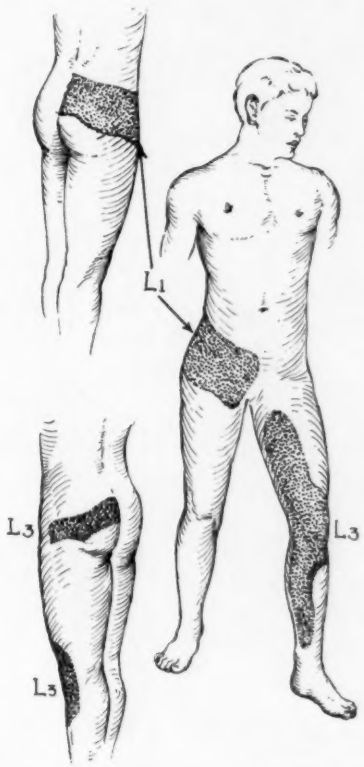


Fig. 3.—The first (*L1*) and the third (*L3*) lumbar dermatome, after Foerster.

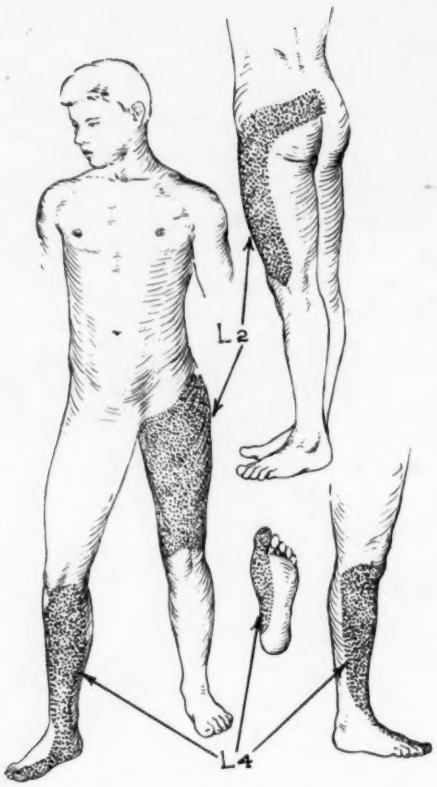


Fig. 4.—The second (*L2*) and the fourth (*L4*) lumbar dermatome, after Foerster.

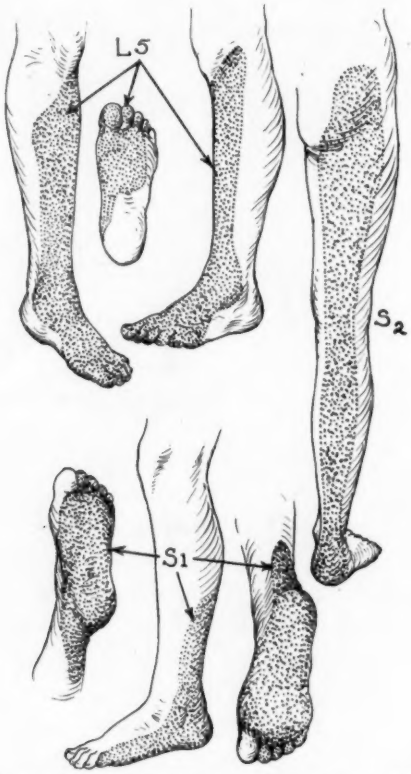


Fig. 5.—The fifth lumbar (*L5*) and the first and second sacral (*S1* and *S2*, respectively) dermatome, after Foerster.

Several points in regard to the use of the scheme may be mentioned briefly: 1. No anesthesia will be found on examination unless two or more segments are physiologically incapacitated. This fact, long recognized, apparently needs reiteration from time to time. 2. Lesions that produce isolated segmental anesthesia, with intact segments above and below, are extremely rare; when they are present, however, the affected segments will be identified by recognition of the lower margin of the uppermost and the upper margin of the lowermost functioning level. 3. The major use of this scheme is in the recognition of a level below which sensory function of the skin is abolished, as met in cases of tumor or injury of the spinal cord. In such cases the configuration of the caudal margin of one of the dermatomes here presented will be found to give the identity of the highest functioning segment.

After some experience with it, Foerster's scheme is believed to be satisfactory. It is recommended to practitioners who have been annoyed to find, after careful sensory examination in cases of segmental sensory disturbance, that their findings have no significance according to conventional charts of innervation.

# SCAPULOPERONEAL AMYOTROPHY

S. DAVIDENKOW
LENINGRAD, U. S. S. R.

In 1927 [1] I observed a peculiar form of muscular atrophy which I regarded as a variety of the Charcot-Marie type, with typical distal distribution of the atrophy of the lower extremities, affecting chiefly the extensor and abductor muscles of the foot. On the other hand, the atrophy of the upper extremities was localized proximally and involved the muscles of the shoulder girdle and partially those of the humerus, whereas the hypesthesias, both of the upper and of the lower extremities, showed a characteristic distal distribution. Observations in 2 cases were in favor of my opinion, the disease in the first being sporadic—none of the relatives had been examined—and in the other familial, the anomaly showing a regular dominant heredity (fig. 1).

The syndrome was conditionally termed scapuloperoneal amyotrophy. In both cases the disease was characterized by partial reaction of degeneration, by a tendency of the toes to form pes excavatus and *pied en griffe* and by a comparatively late onset and exceedingly slow progress, without a tendency to generalization.

Review of a voluminous literature on muscular atrophies showed, however, that similar cases have already been described. It is probable that there belongs here the observation of Eisenlohr,[2] unfortunately reported only in the form of a short article. In this case a family suffered from typical peroneal amyotrophy combined with atrophies of the muscles of the upper extremities, resembling the juvenile myopathy of Erb, with the presence of sensory disturbances. Possibly, the case observed by Sachs [3] also belonged to this category. Two brothers presented typical peroneal amyotrophy accompanied by atrophies of the infraspinatus muscles.

Finally, family A, described by Wohlfahrt,[4] also seems to belong in the same group. The disease showed a dominant inheritance, all 10 members of the family being affected. The atrophy slowly became generalized and gradually reached the muscles of the thighs; the patellar reflexes disappeared; furthermore, the muscles of the trunk and the

1. Davidenkow, S.: Ztschr. f. d. ges. Neurol. u. Psychiat. **107**:259, 1927.
2. Eisenlohr, C.: Neurol. Centralbl. **8**:564, 1889.
3. Sachs, B., cited by Hoffmann, J.: Deutsche Ztschr. f. Nervenh. **1**:95, 1891.
4. Wohlfahrt, S.: Acta med. Scandinav. **63**:195, 1926.

distal parts of the upper extremities were affected, but sensation remained undisturbed. Thick, fleshy lips, typical of myopathies, were characteristic of the family.

New data suggest that one is dealing with a peculiar disease, the main clinical symptoms of which continually recur in stereotyped form. Thus, Oransky,[5] of Leningrad, described 3 families in all of which there were dominant transmission and similar distribution of muscular atrophies. In these cases no sensory disturbances were found. In a series of cases the muscles of the face were involved, thus permitting Oransky to conclude that, in spite of the presence of partial reaction of degeneration in some of the patients, in the main this disease is not a modification of the amyotrophy of Charcot and Marie but a variety of progressive muscular dystrophy. He observed many cases of the rudimentary form of the disease in these families.

In 1929 I[6] described family Z in which the disease was typically reproduced, i. e., highly developed in the person examined and rudi-

Fig. 1.—Family G, in which the person examined presented a typical picture of scapuloperoneal amyotrophy.

mentary in his several relatives. The typical distribution of the atrophies and hypesthesias was general in this family, the orbicularis oris muscle being also involved. Cases of the rudimentary form were characterized by atrophies of slight degree, localized either in the anterolateral part of the skin or in the shoulder girdle, sometimes in both these groups of muscles.

Serebryanik[7] observed family M in Moscow, the members of which presented the same clinical type. Genealogic study revealed that this family was related to family Z which I described, the patients being cousins (fig. 2).

The clinical picture in the branch of the family described by Serebryanik coincided closely with my findings. The history of older generations of this family, from which the two affected branches arose, disclosed no disease. However, it may be assumed that among the

5. Oransky, W.: Deutsche Ztschr. f. Nervenh. **99**:147, 1927.
6. Davidenkow, S.: Ztschr. f. d. ges. Neurol. u. Psychiat. **122**:628, 1929.
7. Serebryanik, B.: Nevrol. i genet. **1**:295, 1936.

members considered as healthy there may have been a certain number of cases of the rudimentary form.

In 1933 I [8] described family Sn, in which father and daughter were affected (fig. 3). Owing to the appearance of new symptoms, this family demonstrated the possibility that the disease may have a very mild course, accompanied, nevertheless, by pronounced reaction of degeneration and fibrillary twitching of the muscles undergoing atrophy. Another family, K, suffering from the same disease, I described in collaboration with Krasnoshapka; [9] there were 7 affected members in

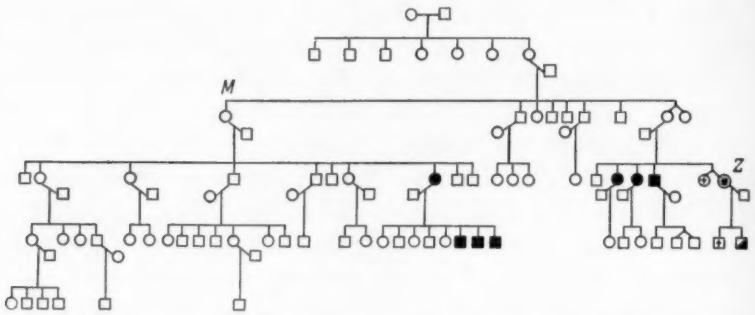


Fig. 2.—Family *Z*, described by me, and family *M*, described by Serebryanik. The son of the person examined in family *Z* was apparently becoming affected. In both branches the course of the disease was similar.

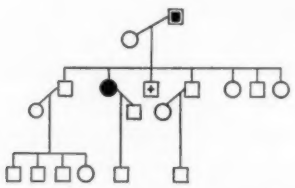

Fig. 3.—Family Sn. A disease of late occurrence and mild course, from which the father was suffering, was rudimentary in the daughter.

three generations (fig. 4). The family appeared to be in no way related to those described previously. In all cases the disease was typical. The atrophy of the lower extremities, even in the mother, aged 57, of the person examined, did not extend proximally beyond the crural muscles, while that of the upper extremities extended distally only to the humerus. The orbicularis oris muscle was involved in this family, as well as in certain cases previously observed.

8. Davidenkow, S.: Sovet. psichonevrol. **9**:9, 1933.
9. Davidenkow, S., and Krasnoshapka, A.: Nevrol. i genet. **2**:247, 1936.

Finally, in 1936, an observation on a family was published by Kulkova,[10] in which the person examined, his sister and his niece were affected (fig. 5). Although the condition of the last 2 patients was rudimentary, the main symptoms—sensory disturbances—were clearly defined. A new feature in this observation was of interest: perioral analgesia and thermoanesthesia accompanied by slight atrophy of the orbicularis oris muscle.

## CLINICAL FEATURES

These observations permit me to give a general characterization of this peculiar form of progressive muscular atrophy.

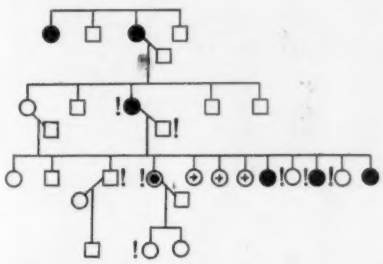

Fig. 4.—In family K (Davidenkow and Krasnoshapka) the patients personally investigated are marked by exclamation points, and persons who died in infancy, by crosses.

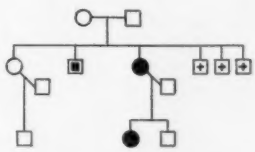

Fig. 5.—Family U, described by Kulkova. The sister and the niece of the person examined had rudimentary forms of the disease.

The disease starts gradually at the age of about 17 to 20, in some cases as late as at 45. Sometimes it involves simultaneously the upper and the lower extremities; in other cases it begins either in the upper or in the lower extremities. Men suffer as frequently as women. The predominance of women in family K (fig. 4) may be accidental. The hereditary transmission of the disease appears to follow a regular dominant, monofactorial, autosomatic type. The expression of the gene is variable; cases of the rudimentary form occur often and are discovered only after medical examination; the bearers of these slight anomalies do not consider themselves ill. In cases in which the disease is developed the atrophy affects the muscles of the shoulder girdle and the pectoral,

10. Kulkova, E.: Nevropath. **5**:550, 1936.

trapezius, rhomboid and serratus anterior muscles on both sides (fig. 6), the levator scapulae and deltoid muscles usually remaining unaffected. Far less and later do the muscles of the humerus become atrophied. Weakening of the movements of the hand and fingers is rarely observed. Only in 1 case did I observe that the small muscles of the hand became wasted. The muscles of the face often participate, but only slightly; the atrophy is usually limited to asymmetric wasting of the orbicularis oris muscle. Distribution of the atrophy of the muscles of the trunk is seen only in severe, far advanced forms (Wohlfahrt). Typically in the lower extremities there is involvement of the extensor muscles of the

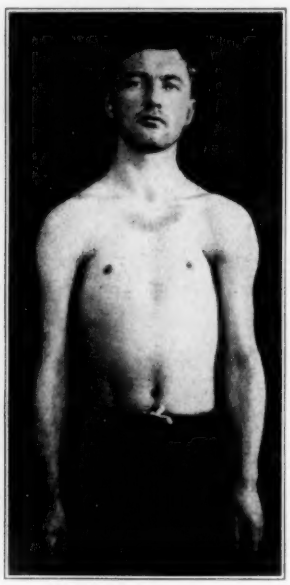

Fig. 6.—A patient with scapuloperoneal atrophy in family K′ (*D* 3 in fig. 8), characterized by caved-in thorax, drooping shoulders, wasting of the muscles of the shoulder and atrophy of the extensor and abductor muscles of the lower extremities. There were no trophic disturbances of the deltoid muscles and the muscles of the forearms.

foot and toes and of the abductor (peronei) muscles (fig. 7); the flexor and abductor muscles of the foot are also often affected. In the majority of cases the atrophy does not extend in a proximal direction, and the muscles of the pelvic girdle remain intact.

Thus, the statement remains valid that in this disease the involvement of the lower extremities resembles the amyotrophy of Charcot and Marie, while the atrophy of the muscles of the shoulder girdle resembles that of the dystrophy of Erb; the development of the atrophy is often

unsymmetric. Through its extension the reflexes become diminished; the tendency to the formation of pes excavatus is present, but both these phenomena are less marked than in the true amyotrophy of Charcot and Marie. Fibrillary twitching and *boules musculaires* are seldom seen; a tendency to slight contraction is observed only in the achilles tendon. Pseudohypertrophy is absent. Electrical examination reveals partial reaction of degeneration in various muscles. The progress of the atrophy is slow. All the patients I have known have preserved the power of independent mobility until old age.

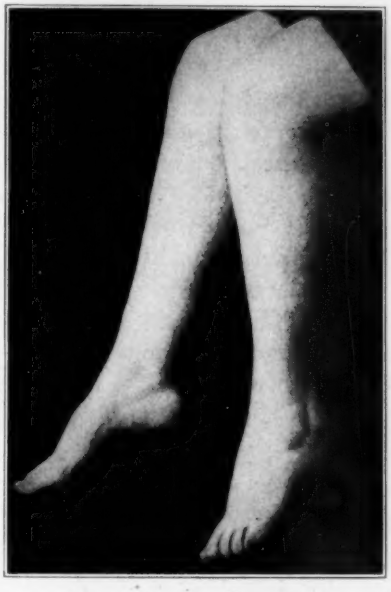

Fig. 7.—Drooping feet due to atrophy of the frontoexternal muscular group of the shin in a case of scapuloperoneal amyotrophy (person examined belonged to family *Z*, fig. 2).

Sensory disturbances are seldom absent. Pains and paresthesias are rare, whereas distinct distal hypesthesias over both the lower and the upper extremities are never absent. Thus, in the upper extremities the localization of the atrophy is the reverse of that of the hypesthesias. The former occupies the proximal and the latter the distal portions. Sensibility to painful and thermal stimuli is chiefly affected, whereas the response to tactile stimuli is better preserved. Deep muscular sensibility is seldom disturbed.

As a rule the hypesthesia fades gradually into the field of normal sensation, but in some cases it is possible to find sharp transverse limits

in the region of the forearm or thigh or at the level of the elbow or knee joint. Perioral hypesthesia, with the same peculiarities, is sometimes found.

Rudimentary forms are characterized only by strictly localized slight wasting and weakening of the muscles, involving those of the shoulder girdle and often those of the lateral part of the thigh simultaneously or of only one of these groups. In rudimentary forms, on the contrary, the hypesthesia may be so pronounced that even the patients themselves notice the symptom.

### PATHOLOGIC CONSIDERATIONS

As no pathologic anatomic investigations have as yet been made, one can offer only presumptions as to the nature of the disorder.

In spite of symptoms suggesting similarity in the localization of the process to that in some forms of myopathy, I am inclined to regard such symptoms as partial reaction of degeneration and, particularly, sensory disturbances as indications of involvement of the nervous system. In that case, the disease would be associated with the amyotrophy of Charcot and Marie rather than with myopathy. On the other hand, it is wrong to regard scapuloperoneal amyotrophy as an accidental variation of the amyotrophy of Charcot and Marie; the two diseases never occur simultaneously in the same family. I have never seen such a combination, nor have I encountered cases in the literature.

My observations on these patients lead me to consider the course of the process as comparatively mild. One often finds that rest in bed with the usual physical therapeutic procedures leads to some improvement. The process in some cases seems to have a tendency gradually to decrease, with the development of long-lasting, stationary defects without further progress. Thus, one is dealing with a peculiar clinical form which cannot be identified either with the humeroscapulofacial myopathy of Landouzy and Dejerine or with the amyotrophy of Charcot and Marie. The question whether the gene concerned is distinct or whether humeroperoneal amyotrophy is related to one of the already known forms is not solved. Genealogic studies over many generations in which many members of a family are affected would contribute to its solution. This would enable one to conclude whether the same clinical type is constantly reproduced throughout such a family or whether transitions from the main type to other clinical forms can be detected. From this point of view family K′ described by Oransky, is of interest. Kulkova and I,[11] in investigating the genealogic tree of a recent patient, unexpectedly discovered that he belonged to the same family, K′. Thus,

11. Davidenkow, S., and Kulkova, E.: To be published.

we were able to supplement the observation of Oransky and to follow the further fate of the patients already investigated by him.

The result was the genealogic chart represented in figure 8. In one branch of the family (the children of *C 1* and *C 2*) 2 patients, *D 1* and *D 3*, with classic forms of the scapuloperoneal type were observed. A sister of the patients, *D 5*, showed slight motor disturbances, with well marked sensory disorders (distal and perioral); she even occasionally failed to experience feeling from burns of the hands. In other branches of the family, on the other hand, the clinical picture was less typical. The condition of *C 4* was very severe; the atrophy had spread over the body (*taille de guêpe* and lumbar lordosis were observed), extending in the upper extremities to the forearms and in the lower extremities in a proximal direction. Typical *boules* were to be seen over the quadriceps and sartorius muscles. Sensation, however, proved to be normal. A sister, *C 13*, of the patient presented a similar picture,

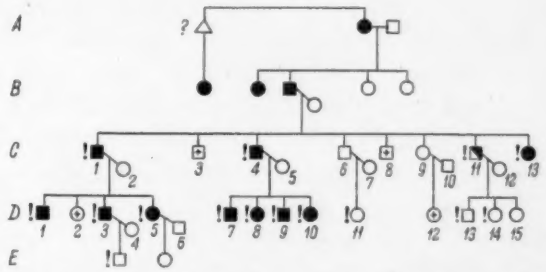


Fig. 8.—Family K′, described by Oransky in 1927 and investigated further by Kulkova and me in 1937. The patients personally investigated are marked with exclamation points. *C 11*, whom Oransky demonstrated as ailing, proved to be normal in our investigation (regressive syndrome).

with the following differences: Hypesthesias were present, and the peripheral nerves when palpated appeared thickened and of unusual cartilaginous solidity. Subsequently, the condition in both these cases approached the facioscapulohumeral type of Landouzy and Dejerine, with some atypical features. This leads one to inquire whether amyotrophy of the scapuloperoneal type, like that of Landouzy and Dejerine, depends on the action of the same basic gene, splitting, however, in other genotypic surroundings. It may be that scapuloperoneal amyotrophy in certain genotypic surroundings presents clinical variations, deviating from its most frequent clinical expression. So far, I have no data permitting an accurate solution of this question. However, I believe that genealogic investigations, properly carried out, alone can decide whether the peculiar clinical condition scapuloperoneal amyotrophy is due to the existence of an independent genotype.

# TREATMENT OF DISTURBED PATIENTS WITH SODIUM CHLORIDE ORALLY AND INTRAVENOUSLY IN HYPERTONIC SOLUTIONS

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AND
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NEW YORK

The proper treatment of dehydrated patients has not received adequate attention. This is particularly true with regard to excited, disturbed and uncooperative patients; since such patients are often transferred to psychiatric wards and hospitals, the problem of dehydration is of special interest to the psychiatrist. Since the psychiatric division of the Bellevue Hospital admits over 26,000 patients a year and all the general hospitals of New York city transfer noisy, excited and uncooperative medical and surgical patients to this service, it must be apparent that the wards for disturbed patients give one ideal material for such a study. We have attempted, therefore, to study empirically physiologic methods for the treatment of such disturbed patients. Another study based on the results of our treatments is under way to determine some of the theoretic considerations of this problem. For the purposes of this report we shall consider the theoretic side only in its relation to actual treatment.

It is common knowledge that excited and delirious patients often have fever and show signs of dehydration. While both frequently appear at the same time, they may occur separately. We believe that many patients suffer from dehydration, as shown by such clinical signs as dryness of the lips, tongue and skin, scanty urine of high specific gravity and generally lessened secretions, without any elevation of temperature. The occurrence of fever without dehydration we regard as much less frequent.

The explanation that fever in excited and overactive patients is due to a primary disturbance or lesion of the heat-regulating center cannot be accepted. The vague concept that fever is of "psychic" origin is

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Read at the New York Academy of Medicine, Section of Neurology and Psychiatry, April 12, 1938.

From the Division of Psychiatry, the Bellevue Hospital, and the Department of Psychiatry, the New York University College of Medicine.

also rejected, except in the sense that the abnormal mental state may cause physical reactions which in turn bring about a febrile state.

It is our belief that certain conditions are common to all markedly disturbed patients, regardless of the type of mental illness. We think that much of the patient's behavior results from disturbance in the water metabolism, that all these patients are dehydrated and that fever, when not based on an obvious physical disease, is due to dehydration.

We also believe that loss of minerals and salts has a close relationship to the dehydration and often plays a role in its production and that any plan of treatment must take this deficiency into consideration. Sodium chloride is the most important of these salts.

It may be argued that biochemical studies of the blood give little corroboration of these ideas. Without introducing material from an investigation now being undertaken, we wish to point out that, in our opinion, normal findings in the blood do not disprove this concept. We believe that the blood will draw on the tissues in order to maintain normal physiologic proportions and that it will show no abnormality even when there are considerable dehydration and loss of salts in other parts of the body.

Although disturbed, like febrile, patients require additional fluids, they nearly always receive less than the normal amount. It is also a common observation that during the hot months there are many more deaths among delirious alcoholic patients and that fever due to dehydration in nonalcoholic psychotic patients is much more difficult to control, so that death occurs more frequently.

In a study by Talbott [1] of heat stroke among miners, steel workers and others, it was found that tablets of sodium chloride prevent the development of heat prostration and cramps and that the simplest and most satisfactory method of treatment is the forcing of fluids and salt. With this study as a basis, we decided to try the use of sodium chloride and fluids in the treatment of our disturbed patients; it is the result of this attempt that we present here.

In our wards for disturbed patients are the cases of more extreme excitement due to alcoholic and other organic deliriums and to manic-depressive psychoses, schizophrenia and dementia paralytica. Hence this study is concerned only with extreme conditions, since if a patient could be cared for in a quieter ward, the case did not find its way into this series.

We shall discuss first our experiences with the delirious alcoholic patients. In considering how to treat these patients, it was first decided that edema of the brain, which is present at times, should be disregarded

1. Talbott, J. H.: Heat Cramps, Medicine **14**:323 (Sept.) 1935.

and that treatment should be only for acidosis and dehydration.[2] These alcoholic patients had been drinking scarcely any water for a considerable period before the development of the delirium. In addition, acetone was present in the urine. Fluids were therefore forced and the patients were given capsules of sodium chloride to help retain the fluids. Two capsules of sodium chloride, 1 Gm. each, were given every four hours during the first day. Fluids were forced in the form of orange juice, with 1 tablespoonful of sucrose to each glass of orange juice. Other fluids were given only when orange juice was not available, but orange juice constituted the bulk of fluid given all patients. Orange juice was used because it combats acidity, supplies certain minerals, helps prevent or overcome infections and supplies vitamin C, which, as Wortis[3] and his co-workers showed in a study of alcoholic patients in the psychiatric service of Bellevue Hospital, is definitely decreased in the blood and spinal fluid in cases of alcoholic psychoses.

Since the brain has a respiratory quotient of unity, it is believed that it can utilize only carbohydrates. If one accepts McQuarrie's[4] report on a study of diabetic children who ate large quantities of sodium chloride, an increase of salt enables the patient to metabolize more carbohydrates. This is of special significance, since the diabetic type of sugar tolerance curve of the blood occurs frequently in cases of alcoholic delirium and suggests a diabetic type of disorder. This also suggests the use of insulin. We are trying the effect of insulin in a series of cases under conditions of careful control, but are not yet prepared to make any conclusions.

According to the reports by Harrop and his co-workers[5] and others, adrenalectomized animals may be kept alive if fed sodium chloride. It is also known that the liver is often affected in cases of chronic alcoholism and that there may be a deficiency of glycogen which can be made available to the system. This makes it imperative to introduce dextrose into the blood stream at frequent intervals.

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2. Hogan, J. J.: Treatment of Acute Alcoholic Delirium, J. A. M. A. **67**: 1826 (Dec. 16) 1916. Nuzum, F., and LeCount, E. R.: Ability of Brain Tissue to Take Up Water in Delirium Tremens and Other Conditions, ibid. **67**:1822 (Dec. 16) 1916.

3. Wortis, H.; Wortis, S. B., and Marsh, F. I.: The Role of Vitamin C in the Metabolism of Nerve Tissue, Arch. Neurol. & Psychiat. **39**:1055 (May) 1938; Vitamin C Studies in Alcoholics, Am. J. Psychiat. **94**:891 (Jan.) 1938.

4. McQuarrie, I.: Effects of Excessive Salt Ingestion on Carbohydrate Metabolism and Arterial Pressure in Diabetic Children, Proc. Staff Meet., Mayo Clin. **10**:239 (April 10) 1935.

5. Harrop, G. A.; Soffer, L. J.; Nicholson, W. M., and Strauss, M. D.: The Effect of Sodium Chloride on Suprarenalectomized Dogs, J. Exper. Med. **61**:839 (June) 1935.

The delirious alcoholic patients were given medication with paraldehyde (even when necessary to repeat the dose) until they fell asleep. However, many of the patients fell asleep as soon as the sodium chloride and fluids were given them.

Our criteria for delirium were that the patient be disoriented for time and place and have either auditory or visual hallucinations. Most of our patients, in addition to the preceding symptoms, misidentified persons, were confused and had physical signs, such as sucking and grasping. Cases of mild delirious states of a few hours were not included in the series. The presence of a surgical or medical condition did not eliminate the case. In a six months' period prior to treatment (from September 1936 to March 1937), there were 92 cases of alcoholic delirium, in 16 of which death resulted from alcoholism, a mortality rate of 17.3 per cent. During the following eight months (from March 1937 to November 1937), all alcoholic patients in the ward for disturbed patients were treated with capsules of sodium chloride and orange juice. In 37 cases of delirium there were 3 deaths due to alcoholism. This gives a mortality rate of 8.1 per cent, as compared with the previous 17.3 per cent. From November 2 to March 1 we gave the treatment on alternating weeks to the alcoholic patients admitted to the ward for disturbed patients. During the weeks when patients were not treated with sodium chloride, they were subject to ward routine, and fluids were forced. Among the treated patients there were no deaths, and of the untreated patients 2 died. It must be remembered that this group was the most uncooperative of the alcoholic delirious patients in the hospital.

In the case of untreated patients the average time required for the delirium to clear was six days during the first period of control and four days during the second period of control, whereas the treated patients required an average of two and two-tenths days.

This form of treatment is in contrast to that described in previous studies by Piker and Cohn [6] and Cline and Coleman.[7] These authors recommended limitation of fluids, and the latter, spinal drainage. Our rationale for treatment with salts and fluids was based on the fact that the patients were suffering from systemic acidosis and dehydration. That salt helps retain water in the body was demonstrated by the work of Coller, Dick and Maddock [8] with operative patients. The study by

6. Piker, P., and Cohn, J. V.: The Comprehensive Management of Delirium Tremens, J. A. M. A. **108**:345 (Jan. 30) 1937.

7. Cline, W. B., Jr., and Coleman, J. V.: Treatment of Delirium Tremens, J. A. M. A. **107**:404 (Aug. 8) 1936.

8. Coller, F. A.; Dick, V. S., and Maddock, W. G.: Maintenance of Normal Water Exchange with Intravenous Fluids, J. A. M. A. **107**:1522 (Nov. 7) 1936.

Talbott [1] on heat cramps clearly shows the ease with which sodium chloride can be utilized to retain fluids in the body. Our results show that forcing of fluids is definitely beneficial. It was decided that there is a particular advantage in feeding the patients by mouth instead of intravenously because it is easier and less of a nursing problem and the patients seem to do better; moreover, we concluded that as a general principle parenteral treatments should be avoided. It may be thought that patients who cannot retain fluids by mouth would present a special problem. During the period of our study we rarely had a patient suffering from hyperemesis who did not retain orange juice and sugar. Even when patients refused to drink, we spilled some on the mouth, and after tasting it most of them would drink. If they remained uncooperative medication was employed and the fluids were given through a Levine tube.

The patients who recovered included those who were admitted with temperatures as high as 105 and 106 F. One patient was admitted with a temperature of 107 F.; it returned to normal within two days, at which time the patient had recovered. This patient also had sucking and grasping reflexes and nystagmus. Two other patients with temperatures of 105 and 104.8 F., respectively, who also exhibited nystagmus, sucking and grasping, recovered.

We report a case which was being studied intensively as part of another investigation.

REPORT OF A CASE

A. A., a man aged 40, in alcoholic delirium, was treated for five days with large quantities of a 5 per cent solution of sucrose. His condition did not improve; instead, it was thought by all who saw him that the illness would be fatal. The temperature rose to 102.4 F. He had visual and auditory hallucinations and was disoriented for time and place, confused and confabulating. Because of his critical condition it was deemed advisable to try the new method of treatment. We began forcing capsules of sodium chloride and gave him sedatives. In twenty-four hours he was suitable for transfer to the ward for convalescents, which is the quietest ward. At that time he was dull, but no longer reacted to hallucinations. Studies of the blood showed that the chloride content was 100 mg. per hundred cubic centimeters, as compared with 350 mg. for normal blood.

We shall mention, with permission, that the neurosurgical staff of our division noticed that disturbed persons with fracture of the skull and delirium tremens improved with this treatment. Though it has been customary to promote dehydration in cases of fracture of the skull, we disregarded the local condition and treated the patients for the delirium by forcing fluids with sodium chloride. This form of treatment has now been adopted and found useful in cases of fracture of the skull and delirium tremens.

As the problems seemed related, we also studied the question of fever due to dehydration in other psychoses, such as schizophrenia, manic-depressive psychosis and dementia paralytica. Review of the ward records for the previous six months revealed 22 cases of dehydration, in 8 of which the patient died. The patients with dehydration who died had either schizophrenia or manic-depressive psychosis, except for 1 patient with a senile psychosis, who was in the ward for one week and died with a condition diagnosed as dehydration. In the other 14 patients the average duration of the fever due to dehydration was seven days. None of the patients had fever due to dehydration on admission. During the five months from May to September, 2 capsules of sodium chloride, 1 Gm. each, were administered every four hours to patients as soon as fever due to dehydration developed. If the patient was fed with a tube, 1 quart (1 liter) of a physiologic solution of sodium chloride was first administered; after a wait of ten minutes the regular tube feeding was given. Physiologic solution of sodium chloride will remain in the stomach for only from ten to fifteen minutes before being absorbed. More frequent, but smaller, feedings were given to thin or asthenic patients, since they were more likely to regurgitate. Three of the 14 patients had temperatures ranging from 101 to 105 F. on admission, and 3 were found to have had fever at one reading only. The average duration of the fever, on the basis of one reading a day, was one and five-tenths days. There were no deaths during that period.

During the period of five months, from October 1 to March 1, all the patients were given 2 capsules of sodium chloride daily. Thirteen patients had fever due to dehydration, the average duration of the fever being one and seven-tenths days. Of these patients, 8 had fever on admission, and 3 others had elevation of temperature at one reading only. Any patient who had a temperature over 100 F. was included in this study. During this period 3 patients died. One, with schizophrenia, had a temperature of 105 F. on admission. There was a history of ingestion of poison and bloody urine, but in this case neither the laboratory examinations nor the gross postmortem study revealed the type of poison. Another patient with schizophrenia was admitted with a temperature of 102 F. and died six days later. He had subsisted on lemon juice for several weeks prior to admission, and there was a dark brown vomitus from the day of admission. The third patient had dementia paralytica, with a temperature of 103 F. on the fifth day, and died two days later. Roentgenographic examination revealed extensive pneumonic consolidation of both lungs. Thus, there have been an abrupt drop in the duration of fever due to dehydration and a marked decrease in the number of deaths from exhaustion as a result of the use of sodium chloride. Patients who recovered from dehydration

included one with epilepsy and a psychosis, whose temperature rose to 105.3 F., and another with schizophrenia, with a temperature of 104.8 F. It should be noted that our period of study covered the summer months, when fever due to dehydration occurs most frequently and is most difficult to treat.

These results suggest that the occurrence of fever due to dehydration in psychotic patients does not result primarily from involvement of the heat center, but is due to inability to retain fluids in the body. The salt stimulates the patients to eat and drink more. Furthermore, we have found that noticeably fewer patients require tube feeding when treated by this method.

As a general principle, hydration by mouth is better than by the parenteral route. Fluids can be forced in large quantities without any danger to the circulatory system. A study of the charts of patients who had died with elevation of temperature due to dehydration showed that many had been treated with continuous infusions of physiologic solution of sodium chloride. Our results from the oral administration of a solution of sodium chloride suggest that this method has special advantages.

In addition to the method already described, we tried using a hypertonic solution of sodium chloride (300 cc. of a 5 per cent solution) in the treatment of disturbed patients. Silbert's [9] experience with thousands of such infusions has shown that it has little danger. A hypertonic solution of sodium chloride in 5 per cent concentration was used at various times for excited, uncooperative patients. It was found that many of these patients became quiet and more manageable. They would eat and drink. In several cases patients who could not retain tube feedings begged for water before the completion of the infusion of a hypertonic solution of sodium chloride. One patient was particularly interesting in that he had regurgitated all tube feedings and had carbuncles on the hands and face. After treatment with a hypertonic solution of sodium chloride he began to eat, drink and retain nourishment. At the end of three weeks he ate solid food. Schizophrenic patients with conditions closely resembling manic states do not seem to quiet with the treatment. However, it helps them to eat, drink and retain body weight. The treatment used was not the hydrating and dehydrating method of Hassin and Broder.[10]

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9. Silbert, S.: (*a*) Treatment of Thrombo-Angiitis Obliterans by Intravenous Injections of Hypertonic Salt Solution, J. A. M. A. **86**:1759 (June 5) 1926; (*b*) Thrombo-Angiitis Obliterans (Buerger): Results of Treatment with Repeated Injections of Hypertonic Salt Solutions, ibid. **94**:1730 (May 13) 1930.

10. Hassin, G. B., and Broder, S. B.: Intravenous Injections of Hypertonic and Hypotonic Solutions: Their Therapeutic Value in Treatment of Some Mental Disorders, J. A. M. A. **104**:1955 (June) 1935.

The patients received 150 cc. of 5 per cent solution of sodium chloride intravenously the first time, then 300 cc. every other day. Fluids were forced on alternate days. If possible, the patients were kept from drinking for two hours after the infusion, since they seemed to do better if this routine was carried out. It is not clear to us why this should be the case. The solution was given in ten minutes. If it was given slowly they did not become thirsty. On a few occasions we gave 150 cc. of a 10 per cent solution of sodium chloride with satisfactory results when the use of a 5 per cent solution had had no effect.

In 3 cases of schizophrenia to date the condition has cleared with this method of treatment, and the patients have returned to work. Obviously, no definite conclusions can be drawn from these 3 cases, since many other patients did not quiet sufficiently in a month to be discharged. The cases are cited merely as an interesting observation.

After we had started our study, we discovered that in 1935 a hypertonic (20 per cent) solution of sodium chloride was used by Cahane [11] in treating patients who did not eat or drink and who were fearful and depressed. These patients began to eat and drink and reacted favorably to this solution. Cahane expressed the belief that concentration of chlorides is needed for the vegetative centers of the brain. There is a multiplicity of reasons why a hypertonic solution of sodium chloride may be of use in the treatment of disturbed patients. Silbert's [9b] work on thromboangiitis obliterans may be extremely important in that he concluded that he altered the viscosity of the blood and the blood volume, thus affecting the rate of flow of the blood. In view of the work of Looney and Freeman,[12] who expressed the belief that the blood volume of schizophrenic patients is lowered, change in alteration of the viscosity of the blood would be of importance. Furthermore, the current of absorption in the cerebrospinal fluid, as pointed out by Foley,[13] may be important. Torbert and Cheney [14] showed that colloidal osmotic pressures are affected, and, before them, Weed and McKibben [15] showed the dehydrating effect of hypertonic solutions on the brain.

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11. Cahane, M.: Le rôle du métabolisme du chlore dans l'anorexie et la sitiophobie de certains malades, Ann. méd.-psychol. (pt. 1) **93**:193 (Feb.) 1935.

12. Looney, J. M., and Freeman, H.: Volume of Blood in Normal Subjects and in Patients with Schizophrenia, Arch. Neurol. & Psychiat. **34**:956 (Nov.) 1938.

13. Foley, F.: Alterations in the Current of Absorption in the Cerebrospinal Fluid Following Salt Administration, Arch. Surg. **6**:587 (March) 1923.

14. Torbert, H. C., and Cheney, G.: Reduction in Colloidal Osmotic Pressure of Blood Serum After Salt Ingestion, J. A. M. A. **106**:638 (Feb. 29) 1936.

15. Weed, L., and McKibben, P. S.: Pressure Changes in Cerebrospinal Fluids Following Intravenous Injections of Solutions of Various Concentrations, Am. J. Physiol. **48**:512 (May) 1919.

## CONCLUSION

By the use of sodium chloride, either by mouth or by intravenous injection of physiologic or hypertonic solutions, and by forcing fluids we have been able to decrease the death rate of excited and disturbed patients with mental disease. Patients with both organic and functional disturbances were treated, including a special group with alcoholic delirium. It was also found that this method of treatment shortened the period of excitement in the patients so treated. We believe that fever due to dehydration can be prevented or successfully treated by this method.

# ART OF PSYCHOTIC PERSONS

## A RESTRAINT-ACTIVITY INDEX AND ITS RELATION TO DIAGNOSIS

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AND

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Art expression in a normal person tends to show a balance between activity and restraint in the mental state. This is adequately demonstrated in the paintings of such artists as Sargent, Raphael, Reynolds and Rembrandt. In the drawings of a psychotic person, on the other hand, there is definite evidence of a dominance of either activity or restraint. In many such productions this can be observed immediately; in others it must be sought in situations in which the restraint or activity is concealed or overshadowed by other material. Investigation of this material, moreover, appears to reveal a definite correlation not only between certain types of psychoses and artistic productions but also between the activity or restraint exhibited in a series of productions by a patient and the course of the patient's mental illness. In the division of creative therapy at this hospital we have been investigating these factors for several years, and as there is no significant literature dealing with such problems we feel it pertinent to present briefly in this paper certain of our results.

### LITERATURE ON THE ART OF PSYCHOTIC PERSONS

During the past twenty years much has been written about art expression by psychotic persons. Attention, however, has been centered largely on the artistic productions of the schizophrenic patient, perhaps because it has been thought that the art of such patients is interestingly open to symbolic interpretation and analysis. This, coupled with the fact that a schizophrenic person apparently interprets reality in terms of his inner experiences and symbolically according to his individual apperception, has led observers to conclude that the art of the schizophrenic patient is, as Hutter [1] stated, "for the most part a symbolic art."

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From the Division of Creative Therapy, the Boston State Hospital.

1. Hutter, A.: World View of Schizophrenic Persons as Expressed in Their Art, Nederl. tijdschr. v. geneesk. **78**:1306-1323, 1934.

After the early observations of Mohr [2] in 1906 and of Morgenthaler [3] in 1919, Prinzhorn [4] in 1922 laid the foundations of factual research in the art of psychotic persons by his comprehensive study of the drawings of schizophrenic patients. Unfortunately, he and most of those following him concentrated their efforts on the drawings of schizophrenic patients and concerned themselves principally with speculative interpretations of symbolic significance, especially from a psychoanalytic point of view. Among these were Janota,[5] Vinchon [6] and Maschmeyer [7] in 1924, Stertz [8] and Stadelmann [9] in 1927, Lewis [10] in 1928, Merzbach [11] in 1930, Osario [12] in 1931, Helweg [13] in 1933, Claude and Masquin [14] in 1934 and Huot [15] in 1936. Aside from this interpretative approach, Becker [16] in 1934 reported the results of his efforts

2. Mohr, F.: Ueber Zeichnungen von Geisteskranken und ihre diagnostische Verwertbarkeit, J. f. Psychol. u. Neurol. **8**:99-140, 1906.

3. Morgenthaler, E.: Ueber Zeichnungen von Gesichtshalluzinationen, Ztschr. f. d. ges. Neurol. u. Psychiat. **45**:19, 1919.

4. Prinzhorn, H.: Bildnerei der Geisteskranken, Berlin, Julius Springer, 1923; Gibt es schizophrene Gestaltungsmerkmale in der Bildnerei der Geisteskranken? Ztschr. f. d. ges. Neurol. u. Psychiat. **78**:512-531, 1922; Das bildnerische Schaffen der Geisteskranken, ibid. **52**:307-326, 1919.

5. Janota, O.: Art in the Insane, Časop. lék. česk. **63**:262-267 and 308-318, 1924.

6. Vinchon, J.: Art and Insanity, Bull. Acad. de méd., Paris **91**:145-146, 1924.

7. Maschmeyer, E.: Ein Beitrag zur Kunst der Schizophrenen, Arch. f. Psychiat. **78**:510-521, 1926.

8. Stertz, G.: Beitrag zu dem Verhältnis von Kunstschaffen und Geisteskrankheit, Deutsche Ztschr. f. Nervenh. **100**:40-62, 1927.

9. Stadelmann, H.: Bildnerei der Geisteskranken, Psychiat.-neurol. Wchnschr. **29**:499, 1927.

10. Lewis, N.: Graphic Art Productions in Schizophrenia, A. Research Nerv. & Ment. Dis., Proc. **5**:344-368, 1928.

11. Merzbach, A.: Symbolische Selbstzeichnungen aus der Psychose eines Jugendlichen und ihre Verwertbarkeit, Ztschr. f. d. ges. Neurol. u. Psychiat. **127**: 240-251, 1930.

12. Osario, C.: L'expression artistique chez les aliénés, Arch. internat. de neurol. **1**:211, 1931.

13. Helweg, H.: Künstlerische Produktion bei Schizophrenen, Acta psychiat. et neurol. **8**:445-446, 1933.

14. Claude, H., and Masquin, P.: L'évolution du dessin chez un paralytique général avant et après malariathérapie: Contribution à l'étude de l'action des traitements actuels de la paralysie générale, Ann. méd.-psychol. (pt. 1) **92**:356-374, 1934.

15. Huot, V. L.: Note au sujet des peintures et dessins d'un schizophrène Malgache, Ann. méd.-psychol. (pt. 1) **94**:172-186, 1936.

16. Becker, P. E.: Das Zeichnen Schizophrener, Ztschr. f. d. ges. Neurol. u. Psychiat. **149**:433-489, 1934.

to isolate the typical forms drawn by schizophrenic persons and compared these with spontaneous productions by the use of arbitrarily imposed tests. Schottky [17] in 1936, in the report of a case of schizophrenia, called attention to a change in the style of drawings over a period of observation.

## METHOD

The investigations composing this study were all carried out under the same conditions. The patients comprised unselected groups of both men and women

*Restraint-Activity Classification of Psychotic Patients According to Type of Art Expression*

| Diagnosis | Number of Patients | Group R | | Group A | | Group R and A | | Unclassified (Artistic Productions Similar to Those of Normal Person) | |
|---|---|---|---|---|---|---|---|---|---|
| | | Male | Female | Male | Female | Male | Female | Male | Female |
| 1. Dementia praecox | 27 | 1 | 0 | 8 | 18 | .. | .. | .. | .. |
| 2. Manic-depressive psychosis | | | | | | | | | |
| a. Manic | 15 | 0 | 0 | 5 | 10 | .. | .. | .. | .. |
| b. Hypomanic | 7 | 0 | 3 | 1 | 3 | .. | .. | .. | .. |
| c. Depressive | 45 | 9 | 34 | 1 | 1 | .. | .. | .. | .. |
| d. Stuporous | 7 | 1 | 3 | 0 | 3 | .. | .. | .. | .. |
| e. Mixed | 2 | 0 | 1 | 0 | 0 | 0 | 1 | .. | .. |
| 3. Psychoneurosis | 14 | 5 | 7 | 0 | 2 | .. | .. | .. | .. |
| 4. Paranoid condition | 9 | 0 | 0 | 0 | 9 | .. | .. | .. | .. |
| 5. Psychosis with psychopathic personality | 11 | 0 | 0 | 4 | 7 | .. | .. | .. | .. |
| 6. Psychosis with mental deficiency | 9 | 0 | 1 | 1 | 7 | .. | .. | .. | .. |
| 7. Alcoholic psychosis | 3 | 0 | 0 | 2 | 1 | .. | .. | .. | .. |
| 8. Psychosis due to drug addiction | 2 | 0 | 2 | 0 | 0 | .. | .. | .. | .. |
| 9. Psychosis with cerebral syphilis | 3 | 1 | 1 | 0 | 1 | .. | .. | .. | .. |
| 10. Involutional melancholia | 1 | 1 | 0 | 0 | 0 | .. | .. | .. | .. |
| 11. Psychosis due to metabolic disorders | 2 | 0 | 2 | 0 | 0 | .. | .. | .. | .. |
| 12. Post-traumatic personality | 3 | 1 | 0 | 2 | 0 | .. | .. | .. | .. |
| 13. Psychosis with epilepsy | 1 | 0 | 0 | 1 | 0 | .. | .. | .. | .. |
| 14. Undiagnosed psychosis | 7 | 0 | 2 | 2 | 1 | 0 | 1 | 0 | 1 |
| Total | 168 | 19 | 56 | 27 | 63 | 0 | 2 | 0 | 1 |

sent from the wards to the creative therapy department for study. Each patient was ushered into the studio and permitted to do as he pleased. He was treated as if he were a guest, and when, after satisfying his curiosity, he wished to draw he was shown the various mediums and permitted to select his own. Oils, water colors, clay, pastels, charcoal and pencil were available. Usually from 10 to 15 persons were present at a given time. If a patient wished instruction, he

17. Schottky, J.: Ueber einen künstlerischen Stilwandel in der Psychose, Nervenarzt **9**:68-76, 1936.

was kindly but definitely informed that we were interested in what he could do without help. However, if after a drawing had been completed he wished its bad points criticized, he was helped to remove the obstacles that hindered him in carrying out his own ideas in his own way. The choice of the subject matter was likewise left to the patient, and in this manner creative effort was encouraged. In the analysis of the productions four classes of evidence were used: (*a*) productivity—(to be interpreted as quantity of output, scale of drawn forms, mass of color, quantity of detail and size of the rectangle used for drawing), (*b*) design—(to be interpreted as the arrangement of the composition, note being taken of whether or not the arrangement exhibits anxiousness, carefulness, deliberation, expansiveness or exuberance), (*c*) imagery—(to be interpreted as the quality of vagueness, symbolism or literal or intellectual realism shown by the

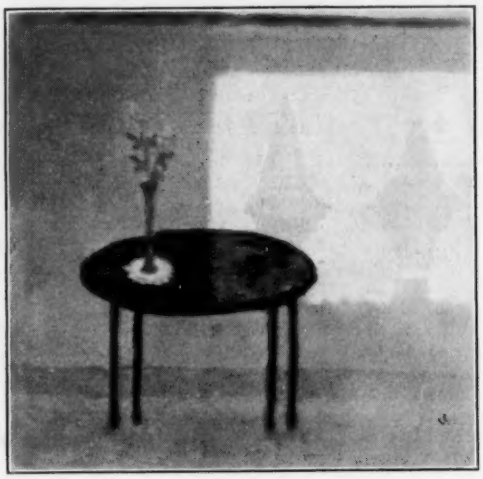

Fig. 1.—Drawing by a patient with a depressive psychosis. The rating of this patient is as follows:

| | | |
|---|---|---|
| Productivity.. | 50 | (normal) |
| Design..... | 30 | (pattern carefully arranged; design not free) |
| Imagery..... | 20 | (much attention to accuracy of forms) |
| Technic..... | 30 | (style deliberate, almost cramped) |
| R-A index.... | 32 | (drawing belongs in group R) |

drawing), and (*d*) technic—(to be interpreted as the mechanical process of production, note being taken of whether the style is cramped, tight, hesitant or uncertain or evinces speed, certainty, fluency or breadth).

Each picture or clay model was then rated in each of these four classes of evidence on a scale of 0 to 100, the rating depending on the amount of freedom shown. The normal control range was established as from 40 to 60. Ratings below 40 were considered as evidence of restraint, and ratings above 60 were considered as evidences of activity. The scores of the four classes of evidence for each drawing were averaged and recorded as the restraint-activity index

(R-A). If the scoring was below 40 the drawing was considered as evidence of a type R (restraint) psychosis, whereas if the scoring was above 60 the drawing was considered as evidence of a type A (activity) psychosis.

## RESULTS

This study consists of an analysis of the artistic productions of 168 patients, of whom 122 were female and 46 were male. The accompanying table shows the incidence of the various psychotic types in the study and the frequency of restraint and activity ratings for each. From this table it is obvious that of 27 patients with dementia praecox, 26

Fig. 2.—Drawing by a patient with a manic psychosis. The rating of this patient is as follows:

| | | |
|---|---|---|
| Productivity.. | 80 | (speed and expansive flux shown; scale of object large) |
| Design..... | 90 | (great freedom; careless arrangement) |
| Imagery..... | 80 | (object freely drawn with little attention to accuracy) |
| Technic..... | 90 | (careless exuberance shown) |
| R-A index.... | 85 | (drawing belongs in group A) |

presented consistent evidence that they belonged to the activity, or A, group, while 1 belonged in the restraint, or R, group. Of the 52 patients with manic-depressive psychoses (depressive and stuporous types) 47 scored below 40 and were placed in the restraint (R) group, and 5 scored above 60 and were placed in the activity (A) group. Of 22

patients with manic-depressive psychoses (manic and hypomanic types), 19 scored above 60 and were placed in the activity (A) group, while 3 scored below 40 and were placed in the restraint (R) group. The patients with conditions diagnosed as paranoid and as psychoses with psychopathic personality without exception scored above 60 and were placed in the activity (A) group. Of the patients with psychoses and mental deficiency, 8 were placed in the activity (A) group and 1 in the restraint (R) group. Of the 14 psychoneurotic patients 12 were placed in the R group, whereas 2, both with conversion hysteria, scored in the A group. The persons with alcoholic psychoses took rating in the A group, whereas those with psychoses due to drug addiction rated in the R group. One patient in a case in which no clinical diagnosis could be made scored from time to time alternately in both groups. In

Fig. 3.—Drawing by a patient with dementia praecox. The rating of this patient is as follows:

| | | |
|---|---|---|
| Productivity.. | 90 | (picture large; space completely filled) |
| Design..... | 50 | (forms on large scale but showing balanced pattern) |
| Imagery..... | 50 | (fairly normal; apparent symbolism to be ignored) |
| Technic..... | 90 | (loose and unhesitating) |
| R-A index.... | 70 | (drawing belongs in group A) |

brief, this table tends to show that the group A type of artistic expression is produced principally by persons with dementia praecox, paranoid conditions, psychopathic personality, alcoholic psychosis and manic-depressive psychosis (manic type) while group R is composed mainly of persons with psychoneurosis, manic-depressive psychosis depressed type and psychosis due to drug addiction.

Figure 1 typifies the drawings of a patient in a state of depression. Figure 2 typifies the drawings of a patient with a condition diagnosed as manic. Figure 3 typifies the drawings of a patient with a psychosis diagnosed as dementia praecox.

When the restraint-activity index of a person is charted for a given period and compared with the clinical course of the mental condition, it is notable that the curve comparisons of the R group are distinctly the reverse of those of the A group. This may be seen in fig. 4. If on the same chart the clinical course of the illness could be plotted, in group R the art curve and the clinical course of the mental condition would tend to be parallel, while in group A they would tend to be in opposition. This would indicate that as the patient in group R gains or loses in mental health his art expression gains or loses in freedom of activity; that as the art expression of a patient in group A grows still more free his mental illness becomes worse, and as his mental illness decreases his art expression acquires evidence of restraint.

## COMMENT

In this brief presentation of certain aspects of our work on the art productions of psychotic patients we have tried to evaluate our results in an objective manner. We realize fully the difficulties and chances of error in attempting this. Yet they cannot approach those resulting from speculation, whether from a psychologic or a mystic point of view, on the symbolic meanings in art. As a matter of fact, purely symbolic art productions have been exceedingly rare in our experience. Patients who have produced art of this sort appear to us to belong in a group of their own, which we do not feel equipped to discuss as yet. Throughout our work we have attempted to discover what type of art productions a given patient will create and whether or not the type remains constant or changes as the mental illness becomes better or worse. It was a source of some surprise to us to find that most persons can be classified continuously in one of two groups—that their art exhibits consistent restraint or consistent activity—and that the person whose psychosis is characterized by artistic restraint will show less restraint as/if his mental condition improves, whereas the person showing dominant activity in his art shows more restraint in it as/if his mental condition improves. Even more surprising to us was the fact that persons with dementia praecox showed the same degree of freedom of activity as persons with manic psychoses and that psychoneurotic persons showed the same restraint in their art as persons with depressive psychoses. This, from the point of view of our study in art, would tend to cast serious doubt on the contention of Bleuler [18] that the psycho-

18. Bleuler, E.: Die Probleme der Schizoidie und der Syntonie, Ztschr. f. d. ges. Neurol. u. Psychiat. **78**:373-399, 1922.

EXPLANATION OF FIGURE 4

Graphs showing the results in the present investigations. The vertical figures represent the restraint-activity (R-A) index. The range of 40 to 60 is considered as normal balance. The horizontal figures represent time in terms of weeks.

The chart marked "case I" shows the R-A indexes of the art productions of a patient with hebephrenic dementia praecox in an early stage, studied for ten weeks. His productions show consistently a high R-A index. The chart marked "case II" shows the R-A indexes of the art productions of a psychoneurotic patient during a period of nine weeks. During this time she was intensively treated and recovered. Her R-A indexes at first showed much restraint, but as she improved the index became progressively more balanced. The chart marked "case III" shows the R-A indexes of the art productions of a patient with a paranoid condition who was studied for twenty-four weeks. Her productions consistently showed evidence of much activity, and at the termination of the study her mental condition was unchanged. The chart marked "case IV" shows the R-A indexes of the artistic productions of a person whose paranoid condition became progressively worse for twenty weeks. His productions showed a progressive increase in activity, and the R-A index progressively increased. The chart marked "case V" shows the R-A indexes of a patient with a psychoneurosis studied for ten weeks. At first her productions showed much restraint, but as her mental condition improved her productions exhibited less restraint and more activity, tending to become balanced when she finally recovered. The chart marked "case VI" shows the R-A indexes of a patient with catatonic dementia praecox, studied for ten weeks. The productions consistently showed much activity, and the activity increased in the period during which he was studied. The chart marked "case VII" shows the R-A indexes of a patient with manic-depressive stupor, studied for twenty weeks. His productions at first showed much restraint, but as his mental condition improved less restraint was noticeable. At the time of his recovery from the psychosis the productions were well balanced. The chart marked "case VIII" shows the R-A indexes of a patient with early paranoid dementia praecox, studied for twenty weeks. His productions at first were fairly well balanced, although they showed some evidence of activity. As the psychosis progressed his artistic productions showed a progressive decrease in restraint with a subsequent increase in his R-A index.

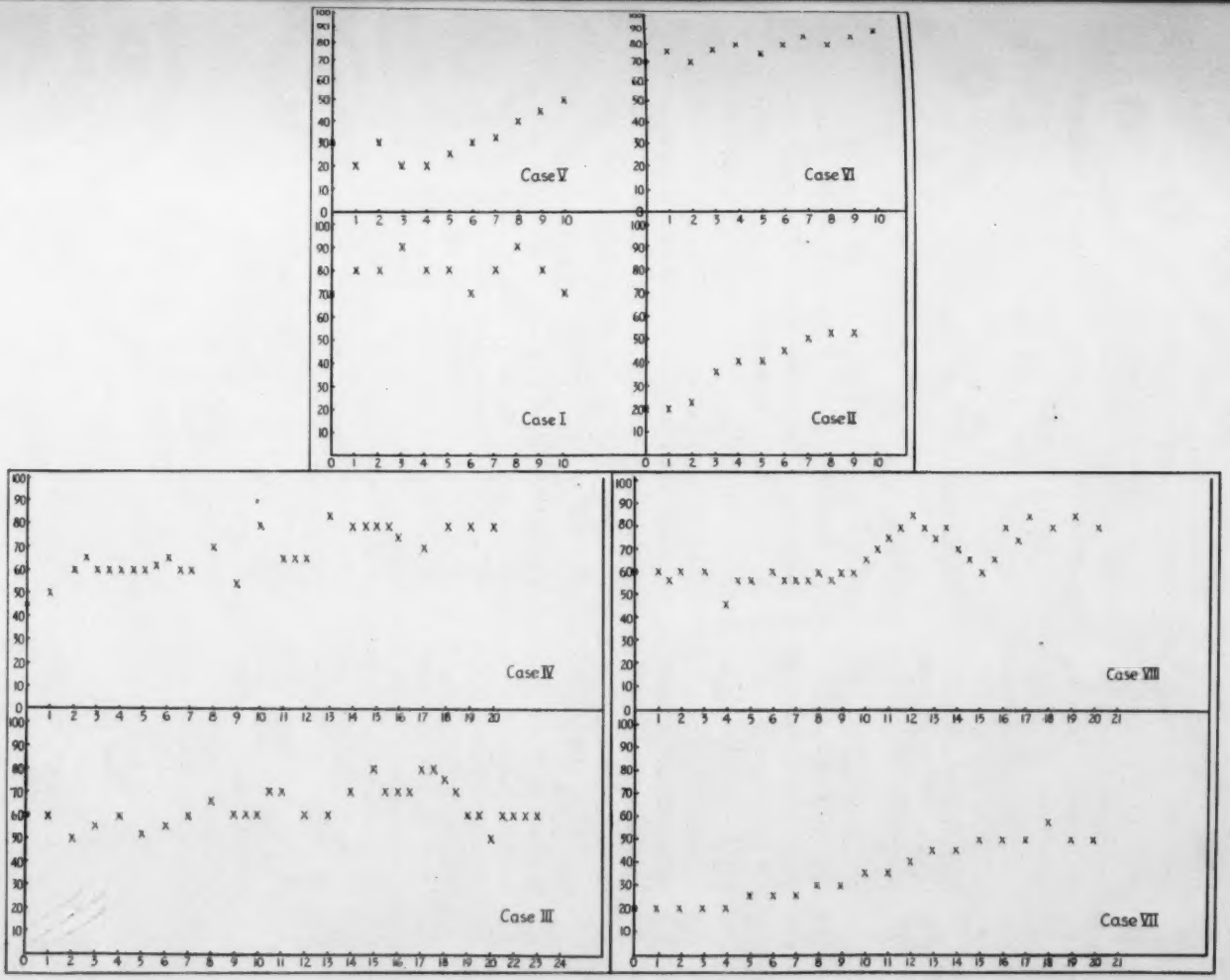
Case V
Case VI
Case I
Case II
Case IV
Case VIII
Case III
Case VII

**Figure 4**

neuroses belong in the same diagnostic category as schizophrenia and to establish some relation between the depressions and the psychoneuroses. Our work would also tend to establish some relation between dementia praecox and the manic type of psychosis. However, these implications are not surprising when one considers that time and again psychoneurosis has been diagnosed as depression and vice versa and that a manic state may be misconstrued easily as a state of schizophrenic excitement. It is also interesting that persons with alcoholic psychoses and those with psychoses due to drug addiction exhibit such opposed artistic productions, since they might be expected to show the same type of R-A index. This, however, brings up the question of the fundamental mechanisms of these two conditions, which cannot be discussed here.

SUMMARY

There appears to be distinct evidence of unbalance between mental activity and restraint in the art productions of psychotic persons. The dominance of restraint is particularly demonstrable in the productions of patients with depressive psychoses, psychoneuroses and alcoholic psychoses, whereas dominance of activity is evidenced in the productions of patients with dementia praecox, a paranoid condition, psychopathic personality, a manic state or drug addiction. As a person exhibiting restraint in his art becomes better or worse mentally, there is a corresponding decrease or increase in his R-A index, whereas in the person showing activity in his art productions the R-A index changes in inverse proportion to the seriousness of his mental illness.

# TREMOR

## PHYSIOLOGIC MECHANISM AND ABOLITION BY SURGICAL MEANS

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Intention tremor resulting from cerebellar lesions can be abolished in subhuman primates by the removal of the precentral cortex (areas 4 and 6 of Brodmann). The demonstration of this fact by Aring and Fulton [1] led to the attempt to relieve a similar incapacitating tremor present in a man. The much older observation that the tremor at rest in patients with parkinsonism is abolished, at least for the duration of the paralysis, by a temporary hemiplegia gave rise to the hope that the tremor at rest also present in this patient would be abolished by a precentral extirpation. In the case reported here both the tremor at rest and that appearing on voluntary movement, which developed after severe cerebral trauma, were abolished by removal of the precentral "arm" area.

### REPORT OF A CASE

G. W. S., a man aged 33, who was referred by Dr. Orthello R. Langworthy and Dr. Lawrence C. Kolb, of the Johns Hopkins Hospital, Baltimore, had been well until the injury which precipitated the present illness. His family and past medical histories contained nothing significant. On May 26, 1936, he was attacked and struck repeatedly on the left side of the head. He was admitted to the South Baltimore General Hospital at 12:30 a. m. on the same day. On admission he was unconscious and flaccid. The left ear was badly lacerated and was bleeding profusely. The pupils were slightly contracted and equal. Roentgenograms of the skull revealed no evidence of fracture. Six lumbar punctures were made. On May 27 the fluid was xanthochromic, and there was a marked increase in globulin

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Read, with motion pictures, at a meeting of the Harvey Cushing Society, Memphis, Tenn., April 23, 1938.

From the Divisions of Neurology and Neurosurgery and of Psychiatry, the University of Chicago and the Otho S. A. Sprague Memorial Institute.

1. Aring, C. D., and Fulton, J. F.: Relation of the Cerebrum to the Cerebellum: Cerebellar Tremor in the Monkey and Its Absence After Removal of the Principal Excitable Areas of the Cerebral Cortex (Areas 4 and 6 a, Upper Part); Accentuation of Cerebellar Tremor Following Lesions of the Premotor Area (Area 6 a, Upper Part), Arch. Neurol. & Psychiat. **35**:439-466 (March) 1936. Fulton, J. F.: The Interrelation of Cerebrum and Cerebellum in the Regulation of Somatic and Autonomic Functions, Medicine **15**:247-306, 1936.

content; there were from 60 to 80 erythrocytes per cubic millimeter. On June 4 there were a faint trace of globulin and 1 monocyte per cubic millimeter, and the pressure was 10 mm. of mercury. Subsequent lumbar punctures revealed nothing abnormal. The patient made a slow but progressive recovery and was discharged on July 7. The diagnosis was severe cerebral concussion, rupture of the left tympanic membrane and laceration of the left external ear.[2]

The patient stated that he knew nothing of what happened until three weeks after the accident. About June 16, on recovering consciousness, he noted difficulty with speech, which was "thick." He knew what he wanted to say but often had trouble in expressing himself properly. This difficulty, although somewhat less severe, had continued up to the present. He also noted considerable weakness of the right arm and leg and difficulty in making these extremities do what he wanted them to. As a result, it was almost impossible for him to write. This difficulty also persisted. On attempting to walk, five and one-half weeks after the injury, he found the right leg to be much weaker than the left. Control over it was poor, and he dragged it as he walked. Although this leg subsequently grew a little stronger, the same type of disturbance persisted. He was discharged from the hospital six weeks after the injury. One week later he awoke one morning to find a spontaneous tremor in the right arm and leg, more severe in the former. This tremor was present in its fully developed state at the onset. To the patient's knowledge, it never changed and never stopped. The tremor, in addition to the preexisting hemiparesis, made it impossible for him to do any work. Auditory acuity in the left ear had been diminished since the injury.

The condition continued unchanged, and in January 1937 the patient was admitted to the Johns Hopkins Hospital, under the care of Dr. O. R. Langworthy. Examination there revealed coarse tremors of the right arm and leg of large amplitude, which "resembled those seen in paralysis agitans." These extremities were hypotonic. Speech was indistinct and explosive. Sensation was intact, and the reflexes were not abnormal. Roentgenograms of the skull were normal. Under Dr. Langworthy's supervision, the patient received scopolamine hydrobromide, 0.0006 Gm. (1/100 grain), three times a day, without any improvement. The medication was discontinued after a week's trial because of the unpleasant side effects. He was then given phenobarbital, 0.032 Gm. (½ grain), three times a day for two weeks without benefit. Bulbocapnine phosphate, 0.3 Gm. (5 grains), was administered subcutaneously. It produced extreme drowsiness but had no effect on the rate or range of the tremor.[3] The patient's condition continued unchanged. He grew despondent and threatened to commit suicide.

*Admission.*—The patient was admitted to the University of Chicago Clinics on Sept. 19, 1937, approximately sixteen months after the injury and fourteen months after development of the tremor.

*Examination.*—He was slender, but well developed and moderately well nourished. He was 173 cm. (5 feet and 9¼ inches) tall and weighed 55.1 Kg. (121¼ pounds). He was right handed. General physical examination gave entirely normal results, except for an extensive, deforming but healed scar of the left ear and blood pressure of 140 systolic and 96 diastolic. The patient was

2. Miss Lillian S. Fleharty, secretary of the South Baltimore General Hospital, furnished this information.

3. Dr. Lawrence C. Kolb, of the Johns Hopkins Hospital, furnished information on the effect of these drugs.

alert and cooperative and had a pleasing personality. He was able to repeat nine numbers forward and five backward. Simple tests in mental arithmetic (e. g., 144 ÷ 3 and 91 ÷ 3) were correctly done. He carried out the usual complicated test commands well. He read well, with good comprehension and without hesitation. Speech was "thick," monotonous, poorly articulated and enunciated and distinctly slurred. There was no evidence that he had any trouble in thinking of what he wished to say, but at times a minor expressive difficulty was obvious. There was no difficulty in comprehension of what was said to him.

The cranial nerves were intact except that there were slight weakness of the right orbicularis oculi muscle and a slight tendency to overaction of the musculature of the right side of the face in emotional movements. There was moderate conduction deafness in both ears, greater in the left. Both tympanic membranes were retracted, more on the left. The disturbance of speech has been noted.

Sensation: Perception of pinprick, cotton, hot and cold test tubes and vibration was everywhere intact. Sense of position and movements was accurate. Two point discrimination, localization of stimuli and recognition of letters written on the skin were accurate. Small coins were easily differentiated with either hand.

Reflexes: The tendon reflexes in the upper extremities (biceps, triceps, radial and finger jerks) were all hyperactive but equal on the two sides. Hoffmann's sign was occasionally present bilaterally. The abdominal reflexes were present, but were less active on the right side. The cremasteric reflexes were active and equal on the two sides. The knee and ankle jerks were hyperactive, only moderately more so on the right side. Babinski's sign was present on the right side on occasion. The Oppenheim, Gordon, Chaddock and Rossolimo signs were not present. The ankle and the patellar clonus were unsustained and equal on the two sides; myotonic irritability as determined by tapping the muscles with a percussion hammer was more marked in the right pectoralis major muscle than in the left.

Strength: Muscular power was good and equal bilaterally in the four extremities, except for slight weakness of the intrinsic muscles of the right hand and of the extensor and flexor muscles of the right elbow. The strength of the grasp as measured by the dynamometer was 115 on the right and 140 on the left.

Muscular development was good throughout. Measurement of the circumferences of the extremities gave the following results:

| | Right, Cm. | Left, Cm. |
|---|---|---|
| Upper part of arm | 23.5 | 23.2 |
| Forearm | 25.0 | 25.0 |
| Thigh | 41.0 | 43.0 |
| Calf | 30.1 | 31.2 |

Coordination: The finger to nose test was performed well on the left side and poorly on the right, but here it was complicated by a tremor, which will be described subsequently. The heel to knee test was performed equally well on the two sides. Rapid alternating movements of the upper extremities, such as rapid pronation and supination and flexion and extension of the wrist and flexion and extension of the fingers, were well performed on the left side, but were more slowly and much more awkwardly executed on the right. Rapid shaking of the foot was performed slightly, if any, faster on the right side. Writing, attempted with the right hand, was completely illegible, but this effort was much complicated by the tremor (fig. 1).

Tone: The patient was an amateur tap dancer. He had since childhood been able to hyperextend the fingers of both hands until they formed an angle of about 45 degrees with the dorsum of the hand. He had also been able to place his feet behind his head. Both these abilities persisted without alteration or difference on the two sides. On passive movement there was little, if any, difference in the resistance in the two upper extremities. In the lower extremities there seemed to be an increase in resistance to passive movement, such as flexion of the knee, on both sides, but slightly more on the right.

Tremor: During waking hours there was a constant coarse, rhythmic tremor involving the entire right upper extremity, including the shoulder, and, to a less extent and much less constantly, the right lower extremity. The tremor had two phases, a tremor at rest and an intention tremor. The left side of the body was not involved. At no time was any tremor of the face, tongue, palate or throat observed.

Tremor at rest: With the patient standing and the arms hanging loosely at the sides, the right shoulder was 3 inches (7.6 cm.) lower than the left; the spine was accordingly curved, with the convexity to the left. Involuntary movements were observed as follows: (1) Fingers. There was little involuntary movement of the last three fingers. The index finger performed rapid, rhythmic flexion and extension, more marked in the distal segments. The thumb performed similar flexion and extension. The movement was principally at the phalangeal-

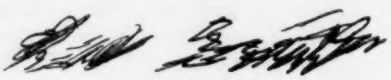

Fig. 1.—Results of the patient's attempt to write his name with his right hand. The influence of the intention tremor is obvious.

metacarpal joint. Occasionally movement of a "pill-rolling" nature, and at other times rhythmic adduction and abduction, were seen. (2) Wrist. Rhythmic flexion and extension of a limited degree (from about 10 to 15 degrees), with the entire hand flopping loosely, were present. (3) Arm. There was no spontaneous pronation or supination of the wrist and no flexion or extension of the forearm at the elbow. The upper portion of the arm and the forearm performed as a unit. There was rhythmic internal and external rotation at the shoulder joint, which at time was associated with slight rhythmic adduction and abduction. This movement was sufficiently intense to shake the upper part of the body. (4) Shoulder girdle. The right scapula oscillated back and forth in a horizontal line. The shoulder itself was moved rhythmically up and down. The involuntary movements in the upper extremity were counted at 200 per minute. (5) Lower extremity. The involuntary movements in the right lower extremity were of much smaller amplitude and less constant than those in the upper extremity. With the patient lying on his back, the pelvis executed rhythmic torsion movements about the long axis of the body. The entire trunk performed similar movements, but they were much less marked. There was no movement at the hip joint. The leg flexed and extended slightly at the knee, and the foot executed slight rhythmic flexion and extension at the ankle. These movements were increased by voluntary movements of the arms, such as extending them horizontally against gravity. There was no involuntary movement of the toes.

On walking the right arm did not swing as did the normal left arm. The amplitude of the tremor in the upper extremity did not appear to be changed,

but the frequency was increased. The muscles of the neck contracted rhythmically to produce a nodding movement of the head. The right leg was circumducted, and the outer anterior part of the foot tended to drag along the floor.

Intention tremor: When the right arm was outstretched to perform the finger to nose test, the tremor practically ceased just as the finger reached the most outstretched point and began its approach to the nose. As the nose was approached the tremor progressively increased in amplitude, until just in front of the nose the hand oscillated rapidly over an area of several inches. The tremor on attempting to write is well illustrated by the reproduction of the patient's writing (fig. 1). There was no demonstrable intention tremor in the lower extremity.

Sleep: All tremor ceased during sleep.

Effect of barbiturates: Because of our previous experience [4] in which both the slow, sinuous movements of athetosis and the rapid, more or less rhythmic movements present in the same case had been temporarily abolished (even for several hours after the patient had recovered consciousness) by administration of a large dose (0.45 Gm.) of pentobarbital sodium by mouth, the effects of various barbiturates were tried in the present case. Langworthy had noted that small but repeated doses of scopolamine hydrobromide and of phenobarbital, as well as a single dose of bulbocapnine, had no effect on the tremor in this case.

On September 23 the patient was given pentobarbital sodium, 0.18 Gm. (3 grains), by mouth in order to obtain satisfactory roentgenograms. While he was under the influence of the drug the tremor was absent; after arousal from this sedative it was present, but seemed somewhat diminished in amplitude, though not in rate.

On September 24 the patient was given 0.4 Gm. of sodium amytal, by mouth at 9:30 a. m. He went to sleep in ten minutes, and all movements ceased. At noon he was awakened by the barber. Tremor was not observed while he was being shaved. When he was spoken to at about 12:05 p. m., tremor appeared in the right hand for a few seconds, then stopped. About 12:10 p. m. he went back to sleep. At 12:30 p. m. he was awakened again. On this occasion tremor was present, but the amplitude was much decreased.

On September 25 0.4 Gm. of sodium amytal was injected intravenously, at the rate of 0.1 Gm. every fifteen seconds. The following brief protocol records the results.

3:10 p. m.: Injection of 0.4 Gm. of sodium amytal begun.

3:11 p. m.: Injection finished.

3:14 p. m.: Somnolent. No tremor, except that when patient moved there was a slow tremor, at the rate of approximately 100 oscillations per minute and with a duration of from five to ten seconds, in the right arm.

3:19 p. m.: Injection of 0.1 Gm. of sodium amytal intravenously.

3:20 p. m.: Sound asleep. Could not be roused by calling his name loudly.

3:25 p. m.: Needle withdrawn from the arm. Patient awakened abruptly. Tremor present.

3:27 p. m.: Sound asleep. No movement.

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4. Bucy, P. C., and Case, T. J.: Athetosis: II. Surgical Treatment of Unilateral Athetosis, Arch. Neurol. & Psychiat. **37**:983-1020 (May) 1937.

3:42 p. m.: Injection of 1 cc. of coramine (a 25 per cent solution of pyridine beta carbonic acid diethylamine) intramuscularly. Tremor soon present.

3:44 p. m.: Sound asleep and motionless.

3:48 p. m.: Site of injection of coramine massaged. Opened his eyes. Spoke. Tremor promptly appeared.

3:50 p. m.: Dozing. Tremor present intermittently.

On September 27 the patient was given 7½ grains (0.45 Gm.) of pentobarbital sodium by mouth, in preparation for an encephalogram.

7:45 a. m.: Pentobarbital sodium, 0.45 Gm., given.

8:05 a. m.: Asleep; motionless.

9:00 a. m.: Encephalogram completed. Left extremities rigid; right flaccid. No movement.

9:50 a. m.: Still asleep and motionless.

10:00 a. m.: Chill-like tremor of entire body, more marked on the right side.

10:20 a. m.: "Chill" less severe and gradually became intermittent.

11:15 a. m.: Slight trembling every three or four minutes. All tendon reflexes hyperactive and approximately equal. Hoffmann's sign bilaterally. Sustained clonus on the right.

12:00 M. : Moved head and extremities a little. No tremor.

1:30 p. m.: Patient turned onto his side. No tremor.

2:00 p. m.: Generalized trembling at intervals of from one-half to two minutes; rate 120 per minute.

3:00 p. m.: Asleep and motionless.

3:30 p. m.: Responded when spoken to. Tremor appeared when he was aroused, but disappeared as he fell back to sleep.

6:30 p. m.: Complained of being tired. Still stuporous. Slight tremor on right side only.

12:45 a. m.: Severe headache. Tremor on right side when aroused. Injection of 0.12 Gm. of sodium phenobarbital subcutaneously.

7:30 a. m.: Awake. Sitting up in bed. Severe headache. Tremor on right side present as before encephalographic examination.

Lumbar Puncture: A lumbar puncture was performed on September 20. The initial pressure was 120 mm. of fluid. The fluid was clear and colorless and contained 3 lymphocytes per cubic millimeter. Pandy's test gave negative results. The total protein content was 43.1 mg. per hundred cubic centimeters of fluid. The Wassermann reaction was negative, and Lange's colloidal gold curve was normal.

Laboratory Examinations: The results of urinalysis and the blood count were normal. The Wassermann and Kahn reactions of the blood were negative.

Roentgenograms: Ordinary roentgenograms of the skull revealed nothing abnormal except an area of calcification in the left external ear. The encephalogram was also essentially normal. The ventricles were of usual size, shape and location. There was no evidence of any atrophy of the caudate nucleus or other basal ganglia. The sulci over both hemispheres were slightly more prominent than usual. This may indicate mild diffuse cortical atrophy. No localized abnormality was seen.

*Operation.*—On Oct. 12, 1937, a left osteoplastic flap was reflected, exposing the central area. The cortex appeared to be normal except that the subarachnoid space contained more fluid than is usually seen. This fluid was released. The ether anesthesia was lightened as much as possible and the cortex stimulated with a faradic current, a unipolar electrode being used (fig. 2). The only movement of the lower extremity obtained was abduction of the thigh from stimulation of the uppermost part of the exposed precentral region. Movements of the right side of the abdominal wall, of the right shoulder, the upper portion of the right arm and the right forearm, wrist and fingers, of the right side of the mouth and about the right eye were obtained. On one occasion the patient seemed to vocalize as a result of stimulation, but this was little more than a grunt. The area of representation of these parts of the body was delimited, and the area representing the right upper extremity was extirpated (fig. 3). The extirpation included the anterior wall of the central fissure down to the bottom of the fissure. It extended forward, including the posterior part of the neighboring frontal con-

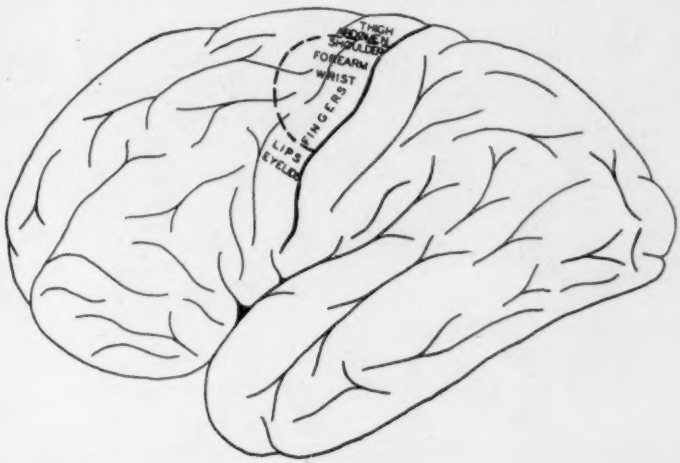


Fig. 2.—Schematic drawing showing the motor representation of various parts of the right side of the body in the precentral gyrus as determined by electrical stimulation. The area of cortex extirpated is outlined by a broken line and includes all the representation of the upper extremity.

volutions. The entire thickness of the cortex and some of the immediately subjacent white matter in this area were removed. The defect so produced measured 2.3 by 3.5 cm. on the surface. It was deepest (1.5 cm.) at the central fissure. The "face" area was carefully spared. The entire dissection was done with sharp instruments. Bleeding was controlled with silver clips. The cautery was not used.

*Microscopic Examination of Cortex Removed.*—The piece of cortex removed from the "arm" area of the precentral gyrus was fixed in alcohol and cut into six blocks; representative sections were stained with thionine and with hematoxylin and eosin. Marked changes were present throughout the cortex removed, although they varied greatly in intensity. There was general reduction in the number of ganglion cells. This reduction was most severe in layers 3 and 5 (there is no layer 4 in the cortex in this region). In some areas the reduction was relatively slight; in others only a few ganglion cells remained. The vast majority of the larger

ganglion cells in the lower part of layer 3 and in layer 5 were abnormal. In most instances these cells were extremely pale. The Nissl substance had largely or entirely disappeared. The cytoplasm was reticulated and vacuolated. In some the nuclei were essentially normal. In others all the nuclear chromatin was gone except the nucleolus, and in some even this stained faintly. In a few instances the nuclear membrane had disappeared, and only a faintly staining nucleolus in a matrix of practically unstained reticulated cytoplasm was seen. Many of the ganglion cells had apparently entirely disappeared; others were represented only by a few fragments of the cell surrounded by the usual glia satellites. In a few large ganglion cells the Nissl substance, except for a ring at the periphery, had been replaced by yellowish green lipochrome pigment. A few ganglion cells, particularly in the more superficial parts of layer 3, were narrow and relatively densely stained and had long, tortuous apical processes.

The glia cells appeared normal. It was easy to imagine instances of satellitosis and neuronophagia, but no unquestionable example of either was observed. The intracerebral vessels were normal.

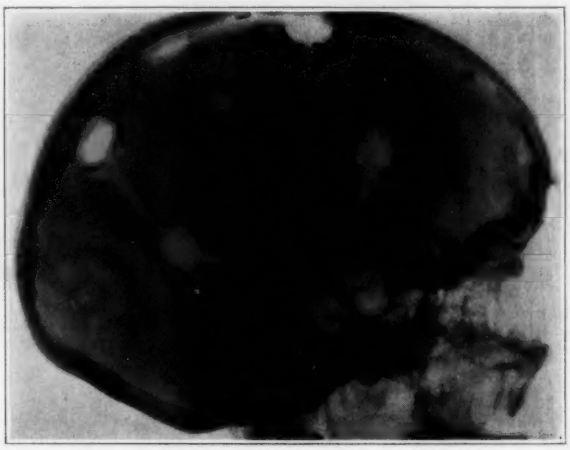

Fig. 3.—Lateral roentgenogram of the skull taken after operation. Silver clips applied to the margin of the defect produced at operation outline the area of extirpation. These are indicated by a ring of crosses. The other clips were applied to the dura mater.

The pia-arachnoid membrane was markedly but irregularly thickened by fibroblastic proliferation. For the most part, it showed no evidence of inflammation. In a few places moderate infiltration with polymorphonuclear leukocytes and lymphocytes was seen. It was impossible to determine how much was the result of surgical trauma, as similar collections of leukocytes were seen at points along the line of incision in the cerebral substance and areas of hemorrhage, obviously of recent and traumatic origin, were prevalent.

*Postoperative Course.*—The patient recovered consciousness soon after the operation. There was no tremor anywhere. There were mild weakness of the right lower part of the face, complete paralysis of the right upper extremity with definite spasticity in the flexor muscles and very mild forced grasping. The patient was able to move the right thigh and leg slightly, but the foot and toes were paralyzed. There was extensor spasticity in that leg, with ankle and patellar clonus, hyperactive tendon reflexes and Babinski's sign. Sensation was not disturbed.

On the day following operation there was slight weakness of conjugate deviation of the eyes to the right. The state of the hemiparesis was unchanged. Speech was less well articulated than before operation, and by evening there had developed a complete expressive (motor) aphasia, which began to disappear on the eleventh day after operation and within two days thereafter had returned to the preoperative condition.

The spastic hemiplegia grew worse for a short time. By the third postoperative day the facial weakness was less marked and soon practically disappeared. On the sixteenth day after operation movement returned to the wrist, and the hemiplegia progressively improved thereafter. The patient began to walk on the twenty-sixth day after operation.

The patient was discharged on December 20, sixty-nine days after the operation. No tremor had been present at any time since operation, either at rest or on movement. The right shoulder drooped as before the operation; the arm hung loosely at the side and tended to flop, but did not swing normally when he walked. There was no posturing of the right arm other than that imposed by gravity, except that the fingers were semiflexed. He did not lift the right foot as high as the left and limped slightly. There was marked weakness of all muscles in the right upper extremity. He could abduct the arm to about 45 degrees and move it forward and backward at the shoulder to about the same extent. He could flex and extend the elbow fully and pronate the wrist fully, but supination was limited to about 45 degrees. He could extend the wrist about 10 degrees and flex it 20 degrees. He could flex and extend all digits fully, but was unable to move any one digit independently of the other four, though he could flex and oppose the thumb and index finger while moving the others little. He was unable to hold a pencil or button his clothes. He could grasp a glass and lift it to his lips, but could not manipulate it well enough to drink from it.

There was moderate clasp knife rigidity at the elbow, greater on extension than on flexion of this joint. Resistance at the wrist was similar, but was much less marked in the fingers, in which it was also greatest in the flexor muscles. All movements were possible in the lower extremities, though the right leg was slightly weaker. There was no incoordination or increase in resistance to passive motion. All tendon reflexes were hyperactive on the right side. The Hoffmann, Rossolimo, Mendel-Bechterew and Babinski signs were present. All abdominal and cremasteric reflexes were present and active. Sensation was intact everywhere except for loss of tickling sensation on the sole of the right foot.

Since his discharge, Dr. Lawrence C. Kolb has repeatedly reported the complete absence of all tremor and continued improvement of the paralysis of the right arm.

When the patient was last heard from on Jan. 2, 1939, almost fifteen months after the operation, the tremor was still completely absent, even though he was still unemployed, was experiencing great difficulty in obtaining what he believed to be adequate financial assistance and was having considerable domestic difficulty. All these difficulties would seem adequate to cause a recurrence of the tremor were it on a functional basis, as an editor of a neurologic journal unreasonably declared. After persistent effort he had retrained his right hand until he could tie his shoes, but it was not otherwise useful.

*Electrical Records.*—Electroencephalograms revealed nothing unusual.

On September 21, prior to operation, electromyographic tracings were made from the upper portion of the arm and the forearm on each side. These were made by wrapping the part under examination at either end with gauze moistened

with saline solution and leading off from these gauze electrodes through suitable amplification to a moving iron oscillograph. In the electromyograms obtained from the upper portion of the right arm and right forearm two types of electrical phenomena were seen. There were coarse fluctuations of variable amplitude but relatively constant frequency which were synchronous with the tremor and were undoubtedly due to movement of the gauze electrodes on the extremity. They were not direct electrical effects from the muscles. They served, however, to record the tremor in a graphic manner. On this occasion the rate of the tremor recorded from both the forearm and the upper part of the arm was 200 oscillations per minute. In addition, considerable irregular electrical activity of slight amplitude was visible in the tracing obtained from the forearm. This, in all probability, represented actual muscular activity responsible for the tremor. In the left upper extremity there was neither tremor nor muscular activity. At the same time tracings were also obtained from the legs. No electrical activity was obtained from the left leg, and only occasionally was a tracing of the tremor at approximately 220 oscillations per minute obtained from the right leg. On September 30 additional records were obtained in the same manner. They were similar to those just described except that the rate was 180 per minute and the tracing obtained from the upper part of the right arm revealed much muscular activity, in addition to the tremor.

As these rather crude electrodes recorded simultaneously from a large number of muscles and also recorded the tremor, a change was made to more satisfactory electrodes. These consisted of silver disks, 1 cm. in diameter, which were applied to the skin with "electrode jelly" (Cambridge) and held in place by collodion. They recorded much more distinct electrical effects from the muscle and reduced the "tremor effect" to a minimum (fig. 4). These electrodes were placed over the flexor carpi ulnaris muscle, but there could be no assurance that the electrical effect recorded originated in this muscle exclusively. In addition, the tremor was simultaneously recorded by sending a beam of light across the right wrist and directing it on a photoelectric cell. The resultant alteration in amount of light caused by the rhythmic tremor produced a corresponding fluctuating electrical current from the photoelectrical cell, which was suitably amplified and recorded by means of the oscillograph (fig. 4).

Records were taken in this manner prior to operation, on October 6 and 12. The rate of the tremor was 200 per minute on October 6 (fig. 4 *A*). On October 12 (fig. 4 *B*) the rate varied from 200 to 240 per minute. The bursts of electrical activity were synchronous with the oscillations of the wrist.

Tracings were made seventeen days (October 29) and two months (December 14) after the operation (fig. 4 *C* and *D*). These tracings revealed no electrical activity in the muscles, and there was no tremor in the tracings made with the photoelectric cell.

*Surface Temperature.*—On October 11 the temperature of the skin as measured with a thermocouple was not significantly different on the two sides of the body. With the room temperature at 76 F. (24.4 C.), the temperature of the skin of the face averaged 33.5 C. (92.3 F.); over the upper extremity it varied from 33 C. (91.4 F), on the forearm, to 29.8 C. (85.6 F.), on the little finger; over the lower extremity it varied from 32.5 C. (90.5 F.), on the leg, to 29.4 C. (84.9 F.), on the little toe. With the room temperature at 62 F. (16.6 C.) the temperature of the skin was 28.2 C. (82.8 F.) on the forehead, 30.3 C. (86.5 F.) on the cheek, 29.8 C. (85.6 F.) on the forearm, 22.3 C. (72.1 F.) on the little finger, 28 C. (82.4 F.) on the leg and 23.7 C. (74.6 F.) on the small toe.

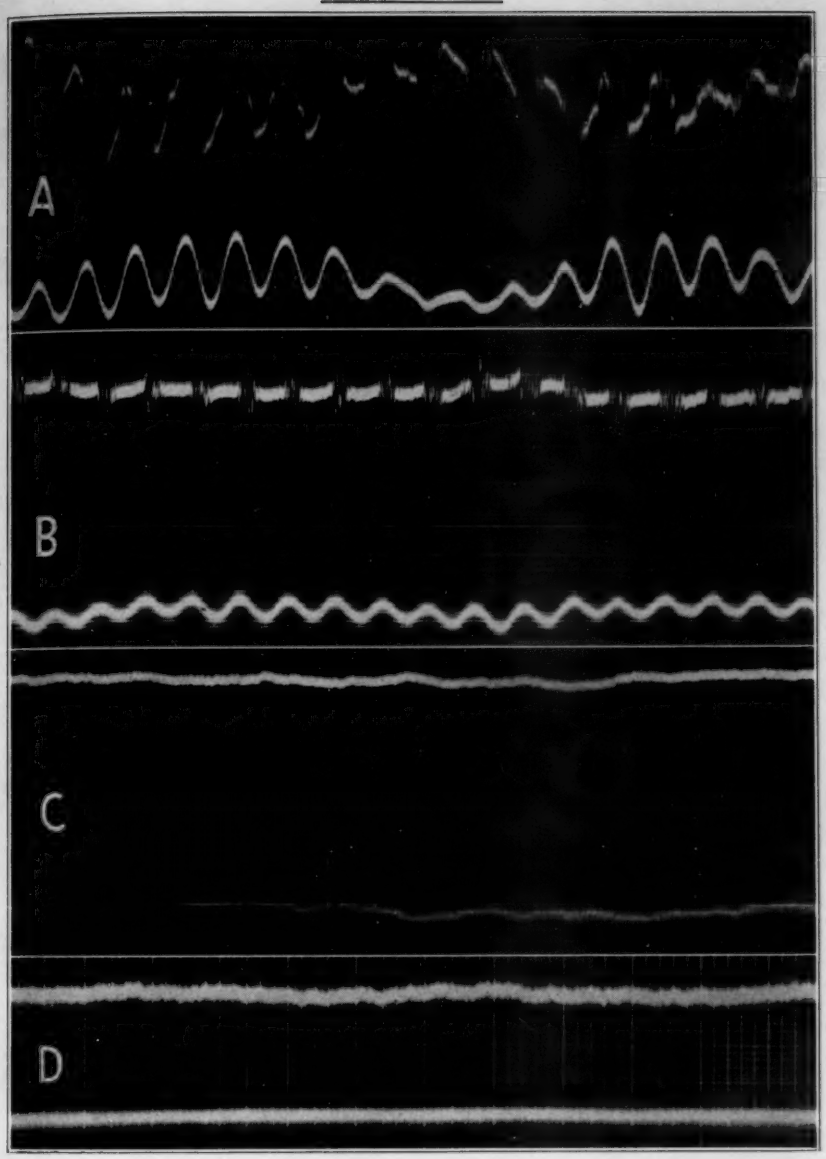


Fig. 4.—An electromyogram made with silver electrodes is the upper tracing in each figure, 1 cm. of deflection indicating 0.3 millivolt. A photoelectric cell record of the tremor is the lower tracing in each figure. Time for *A*, *B* and *C* is shown just above *A;* that for *D* is shown on the tracing, each small subdivision indicating one twenty-fifth second. All tracings were from the right forearm. *A* and *B* were taken before operation, on October 6 and 12 respectively, and *C* and *D*, after operation, on October 19 and December 14 respectively. After operation there was no electrical activity in the electromyogram and no evidence of tremor in the record from the photoelectric cell. All tracings were taken with the arm "at rest," that is, without voluntary movement.

At 5 p. m. on the day of operation, six hours after the operation was terminated, with the room temperature at 24.6 C. (76.4 F.), the surface (skin) temperature was measured with a thermocouple. Over the upper extremities all readings were consistently lower on the right side, the difference ranging from 0.3 C. (0.5 F.) on the forearms to 1.9 C. (3.4 F.) on the middle fingers (table). Over the lower extremities all readings were consistently higher on the right side, the difference ranging from 0.1 C. (0.2 F.) on the legs and dorsa of the feet to 0.7 C. (1.3 F.) on the little toes.

The following day at 7:30 a. m., with the room temperature at 75 F. (23.9 C.), the readings on the right upper extremity, except for the middle finger, were lower than those on the left, though to a much less degree than on October 12. The other readings were from 0.1 to 0.4 C. (0.2 to 0.7 F.) lower on the right. On the right lower extremity the surface temperature was from 0.1 to 0.5 C. (0.2 to 0.9 F.) higher, except for the sole of the foot and the middle toe, which were 0.3 and 0.5 C. (0.5 and 0.9 F.), respectively, cooler than the corresponding areas

*Differences in Surface (Skin) Temperatures on the Two Sides of the Body* *

| | Preoperative Temperatures October 11 | | Postoperative Temperatures | | | |
|---|---|---|---|---|---|---|
| | | | October 12 | October 13 | | November 7 |
| | | | 5 p. m. | 7:30 a. m. | 5 p. m. | |
| Room temperature | 24.4 C. | 16.6 C. | 24.6 C. | 23.9 C. | 16.6 C. | 20.5 C. |
| Forearm | 0 | +0.6 | −0.3 | −0.4 | +0.5 | −0.1 |
| Dorsum of hand | −0.1 | +0.3 | −0.9 | −0.2 | +0.6 | +0.8 |
| Palm | −0.7 | +0.3 | 0 | −0.1 | +0.9 | +0.2 |
| Thumb | +0.4 | 0 | −1.5 | −0.1 | 0 | −1.0 |
| Middle finger | +0.3 | 0 | −1.9 | +0.2 | +0.6 | 0 |
| Little finger | +0.2 | −0.1 | −0.5 | 0 | +1.3 | +0.8 |
| Leg | −0.5 | −0.1 | +0.1 | +0.1 | +0.5 | −0.7 |
| Dorsum of foot | +0.4 | +0.1 | +0.1 | +0.1 | +0.2 | 0 |
| Sole | +0.1 | +0.3 | +0.3 | −0.3 | +0.3 | 0 |
| Large toe | +0.5 | 0 | +0.5 | +0.1 | +0.7 | +0.2 |
| Middle toe | +0.1 | −0.1 | +0.2 | −.05 | +1.7 | −0.4 |
| Little toe | +0.6 | +0.8 | +0.7 | +0.5 | +1.3 | 0 |

* The figures recorded in the table indicate the difference between the surface temperatures on the right side of the body and those on the left. Thus, +0.5 indicates that a given point on the right extremity was 0.5 degree C. (0.9 degree F.) warmer than the same point on the left.

on the left side. That afternoon, at 5 p. m., readings were again made. The room temperature was 16.7 C. (62.1 F.). The surface temperature of both the upper and the lower extremity was uniformly higher on the right side. The difference on the two sides varied from 0, on the thumbs, through 0.2 C. (0.4 F.), on the dorsa of the feet, and 0.6 C. (1.1 F.), on the dorsa of the hands and on the middle fingers, to 1.3 C. (2.3 F.), on the little fingers, and 1.7 C. (3.1 F.), on the middle toes. Readings made on November 7, approximately four weeks after the operation, showed no consistent changes. There was no difference between the temperatures on the forearm, middle finger, dorsum and sole of the foot or little toe on the two sides. The other readings varied as widely as being 1 C. (1.8 F.) lower on the right thumb and 0.8 C. (1.4 F.) higher on the dorsum of the right hand and little finger. In the lower extremities the right leg was 0.7 C. (1.26 F.) cooler, and the right large toe, 0.2 C. (0.36 F.) warmer.

## COMMENT

*Diagnosis.*—There can be little doubt that the condition in this case resulted from the severe cerebral trauma received on May 26, 1936.

The nature and location of the pathologic change are at best only a matter of speculation. The encephalogram demonstrated no abnormality. Although microscopic examination revealed marked fibroblastic hyperplasia of the leptomeninx and severe degeneration of the ganglion cells of the precentral region of the cerebral cortex, it is not possible to establish these changes as those which released the tremor, though it is likely that the cortical degeneration was responsible for the right hemiparesis and the disturbance in speech, which were present after the accident and prior to the operation. It is easy to pass this off as an instance of damage to the basal ganglia or other subcortical structures, but impossible to establish the presence of such a lesion or lesions. It is also possible to classify this case as an instance of traumatic unilateral parkinsonism, but such a diagnosis is not entirely satisfying. It is true that the tremor at rest, although coarser than one usually sees with paralysis agitans, was not unlike that present in this condition. The rate of from 3 to 4 oscillations per second (180 to 240 per minute) is not greatly different from the rate usually given for the tremor of parkinsonism. Lindsley,[5] in a study of several cases of paralysis agitans, found that the rate varied from 4 to 7 per second, with an average frequency of 5.3 per second. In one instance, case 8, in which following a cerebral injury a tremor was present at rest but absent during voluntary movement, the frequency was 5.5 per second. In our case there was a trace of "pill rolling," although that was not the predominant movement of the fingers. There was none of the rigidity or slowness characteristic of the usual sufferer from shaking palsy. In spite of this, however, the tremor at rest had much similarity to that in cases of parkinsonism. In one other respect they were similar, the almost complete cessation at the beginning of each voluntary movement. The severe intention tremor which followed and its crescendo-like increase in intensity as voluntary movement was persisted in were quite unlike what is usually seen in the condition which James Parkinson[6] so accurately described. It is true that intention tremor is not a stranger to that syndrome. In fact, Patrick and Levy[7] stated that an intention tremor was present in 13 per cent of their 140 cases. Even when present, however, an intention tremor rarely occupies the outstanding place in the symptomatology of paralysis agitans that it did in this

5. Lindsley, D. P.: Electromyographic Studies of Neuromuscular Disorders, Arch. Neurol. & Psychiat. **36**:128-157 (July) 1936.

6. Parkinson, J.: An Essay on the Shaking Palsy, London, Sherwood, Neely & Jones, 1817; in Ostheimer, A. J.: A Bibliographic Note on "An Essay on Shaking Palsy," by James Parkinson, M.D., Member of the Royal College of Surgeons, Arch. Neurol. & Psychiat. **7**:681-710 (June) 1922.

7. Patrick, H. T., and Levy, D. M.: Parkinson's Disease, Arch. Neurol. & Psychiat. **7**:711-720 (June) 1922.

case. Thus, one cannot satisfactorily draw too close an analogy between the condition recorded here and parkinsonism. Nor would such an analogy prove of any great value in placing the lesion in this case, for the battle still rages as to whether the lesion responsible for parkinsonism is in the globus pallidus, the substantia nigra or elsewhere.

*Results of Extirpation.*—Abolition of Tremor: Complete abolition of tremor both at rest and on voluntary movement is, of course, the result sought and the one in which we were most interested.

When this case first came under consideration, the advisability of attempting to relieve the patient of his tremor by extirpation of the precentral region was in considerable question. The decision to make the attempt was influenced by three sets of facts: our experience with a similar operation in a somewhat, but not entirely, similar case reported previously; observations that the development of hemiparesis as the result of a cerebrovascular accident in cases of parkinsonism abolishes the tremor, at least temporarily, and the experimental observations of Fulton and his co-workers on the influence of precentral extirpations on tremors resulting from cerebellar lesions.

In the case of R. E. W. previously reported,[4] involuntary movements which resulted from a birth injury had been present in all four extremities from a very early age. They were much the most severe in the right upper extremity. There were irregular movements of a choreoathetoid type and other more or less regular rhythmic movements which were of a rotary character at the shoulder and at times of a "pill-rolling" type in the fingers. The movements were for a few days completely abolished and subsequently much reduced by partial extirpation of the precentral "arm" area (removal of area 6 with preservation of area 4). This experience led us to hope that a more complete extirpation might give even more satisfactory results.

Many authors have stated that the development of a hemiplegia in a patient suffering from paralysis agitans results in temporary abolition of the tremor. Parkinson, in his classic essay,[6] recorded such a case. The patient described in case 6 in his series suffered from a parkinsonian tremor which involved the entire body. He had had an apoplectic seizure resulting in a right hemiplegia, which lasted for two weeks and then completely disappeared. Parkinson stated:

> During the time of their having remained in this state, neither the arm nor the leg of the paralytic side was in the least affected with the tremulous agitation; but as their paralysed state was removed, the shaking returned.

Patrick and Levy[7] recorded a case of bilateral parkinsonian tremor in which, fourteen months after the onset of the tremor, a right hemiplegia developed. With the onset of the paralysis the tremor disappeared on the right side, but gradually returned as the patient

recovered the use of his right arm. It is obvious in both cases that only temporary interference with the function of the cortical innervation of the extremities was present and that so long as those structures remained inactive the tremor was not present. Only with return of function to the corticospinal motor systems did the tremor return. We have found no report of the effect on the tremor of a persistent hemiplegia. Although the tremor in our case was not identical with that present in parkinsonism, it possessed sufficient similarity to that condition to justify hope that permanent destruction of the precentral region might result in persistent abolition of the tremor.

Fulton, Liddell and Rioch [8] demonstrated that removal of the cerebellum in the cat results in a tremor of the extremities that is not present at rest but appears only on voluntary movement, i. e., an intention tremor. They found that removal of one cerebral hemisphere abolished this tremor in the contralateral extremities. More recently, Aring and Fulton,[1] working with monkeys and baboons, have shown that the intention tremor resulting from a cerebellar lesion is temporarily abolished and subsequently diminished by extirpation of area 4, is accentuated by extirpation of area 6 and permanently disappears after removal of areas 4 and 6.

With these experiences and observations as a background, it was decided to remove the "arm" area from the precentral region, including both area 4 and area 6. As the tremor in the leg was insignificant, it did not seem necessary to remove the corresponding "leg" area. The decision to carry out this procedure was further influenced by the fact that Dr. Langworthy had been unable to produce any effect on the tremor with various drugs and that historically there was little reason to believe that drugs would be efficacious. All other surgical procedures (except for actual amputation or severance of the peripheral motor innervation to the part) had likewise failed to abolish or diminish tremor in similar cases. Thus, Putnam [9] and Oldberg [10] both demonstrated that anterior chordotomy, which in their hands proved effective in relieving athetosis, is without effect on the tremor of parkinsonism. Pollock and Davis [11] reported a case of chronic encephalitis with parkin-

8. Fulton, J. F.; Liddell, E. G. T., and Rioch, D. M.: Relation of the Cerebrum to the Cerebellum: I. Cerebellar Tremor in the Cat and Its Absence After Removal of the Cerebral Hemispheres, Arch. Neurol. & Psychiat. **28**:542-567 (Sept.) 1932.

9. Putnam, T. J.: Results of Treatment of Athetosis by Section of Extrapyramidal Tracts in the Spinal Cord, Arch. Neurol. & Psychiat. **39**:258-275 (Feb.) 1938.

10. Oldberg, E., in discussion on Putnam, T. J.: Results of Treatment of Athetosis by Section of Extrapyramidal Tracts in the Spinal Cord, Arch. Neurol. & Psychiat. **39**:258-275 (Feb.) 1938.

11. Pollock, L. J., and Davis, L.: Muscle Tone in Parkinsonian States, Arch. Neurol. & Psychiat. **23**:303-319 (Feb.) 1930.

sonism in which section of the posterior spinal roots on the right side from the fourth cervical to the fourth thoracic segment abolished the rigidity but not the tremor, which at times was even more rapid than before operation. In the same connection, Walshe [12] reported that infiltration of the muscles involved in paralysis agitans with procaine sufficient to paralyze the afferent, but not the efferent, innervation abolishes the rigidity but does not affect the tremor. Delmas-Marsalet, who advocated making lesions in the cerebellum in treatment of parkinsonism, did not refer to the influence of such lesions on the tremor, except in one case, reported with van Bogaert,[13] in which two lesions, one in the dentate nucleus and one in the middle cerebellar peduncle, were produced. In this case the rigidity was diminished, but the tremor was even more marked than before operation.

Nothing in the study of the present case throws any definite light on the nature or location of the pathologic lesion responsible for the tremor. It is true that the cerebral cortex which was removed and examined microscopically was distinctly abnormal, as was the cortex removed in cases of athetosis previously described. But there is no evidence which establishes these changes as essentially related to the development of the tremor. That they may be is not categorically denied. This discussion, however, like the papers on athetosis,[14] is not concerned with the pathologic aspect of the condition. It is concerned only with the physiologic mechanism by which the involuntary movements are produced. We should not belabor this point were it not for the fact that the previous papers on involuntary movements have been grossly misunderstood. In a recent discussion of the dyskinesias,[15] it was stated that we "believe that the involuntary movements in athetosis are due to pathological changes in area 6 of the precentral region." This belief has never been expressed by either of us. We have always said that we do not know where the lesion is located which is responsible for release of the mechanism giving rise to the involuntary movements of athetosis. We now express the same attitude regarding tremor.

That tremor at rest and intention or action tremor are, as Wilson [16] stated, not distinctly separable entities is obvious. It has been previ-

12. Walshe, F. M. R.: Observations on the Nature of the Muscular Rigidity of Paralysis Agitans and on Its Relationship to Tremor, Brain **47**:159-177, 1924.

13. Delmas-Marsalet, P., and van Bogaert, L.: Sur un cas de myoclonies rhythmiques continués déterminées par une intervention chirurgicale sur le tronc cérébral, Rev. neurol. **64**:728-740, 1935.

14. Bucy, P. C., and Buchanan, D. N.: Athetosis, Brain **55**:479-492, 1932. Bucy and Case.[4]

15. Keschner, M.: Dyskinesias, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 10, chap. 14, pp. 307-436.

16. Wilson, S. A. K.: Modern Problems in Neurology, New York, William Wood & Company, 1929.

ously noted that whereas tremor at rest is characteristic of parkinsonism, intention tremor is by no means foreign to this condition. Wilson [16] pointed out that in the disease which bears his name, progressive lenticular degeneration, tremor, although prominent in the resting state, is "increased by voluntary action to a pronounced degree." The same author pointed out that in disseminated or multiple sclerosis both "rest tremor" and "action tremor" occur. Furthermore, Holmes [17] noted that though cerebellar dysfunction is usually characterized by an intention tremor, oscillations of a regular rhythmic sort may be seen when no active innervation is taking place, as when a limb is hanging over a chair or the edge of a bed. In spite of the obvious close relationship between these two types of tremor, certain differences exist. Thus, lesions of the cerebellar efferent pathways in the superior cerebellar peduncles and in their connections in the thalamus commonly give rise to an intention tremor, whereas tremor at rest is thought to be the result of disintegration within the basal ganglia.

Apart, however, from the location of the lesions which destroy structures, removal of the influence of which permits these involuntary movements to appear, there are essential physiologic differences between the two types of tremor. Intention tremor, like cerebellar ataxia, does not appear in simple reflex muscular activity (Walshe). It requires volitional muscular activity for its development. It is not a matter of surprise, therefore, that this type of tremor disappears when the corticospinal mechanism is interfered with, as in the case reported here. It is not so clear, however, why interruption of the function of the corticospinal mechanism should also, and as effectively, abolish tremor at rest, as in the patients suffering from parkinsonism in whom hemiplegia developed and also in our patient. Wilson [16] expressed the unsupported belief that tremor is "a phenomenon of a low physiological order" and thus is not capable of being produced by a mechanism as high in the neurologic hierarchy as the cerebral cortex and the corticospinal fiber system. He accordingly found it necessary to fall back on some other mechanism to explain the abolition of tremor in cases of parkinsonism in which hemiplegia occurs. For this purpose, he chose "diaschisis" of the lower motor neuron, a condition the existence of which was never established and the pathologic or physiologic nature of which was not known. Although he did not define this term, it appears that he referred to the period often called "shock," which is characterized by complete paralysis, flaccidity and absence or marked diminution of all reflexes in the affected part after interruption of the neurons descending from

17. Holmes, G.: Clinical Symptoms of Cerebellar Disease and Their Interpretation, Lancet **1**:1177-1182, 1922.

supraspinal centers by such lesions as section of the spinal cord or a capsular thrombosis or hemorrhage. He said, in discussing his own case:

> A stroke led to its [the tremor's] cessation but only for a time corresponding to complete outfall of function throughout the cortico-spinal system.

Unfortunately, this statement does not agree with the facts.

> In this particular instance (case 1 reported by Wilson and Cobb[18]), a man aged 65 with parkinsonism, presumably due to mesencephalitis syphilitica, had suffered from a coarse tremor of all four extremities and, to a less extent, of the head. On Feb. 19, 1924, he suddenly became comatose and remained in this condition for thirty-six hours. On recovering consciousness, the right arm and leg were very weak, and all tremor had stopped on that side. On March 3, 1924, he was readmitted to the hospital. The right arm had so far recovered that he was able to extend it horizontally and to grasp with it, though it was weaker than the left. Comparable recovery had occurred in the right leg.

Surely, any "diaschisis" of the lower motor neuron which may have existed or any "complete outfall of function throughout the cortico-spinal system" no longer existed; yet there was no tremor.

> The last note in this case was dated March 6, 1924. The tremor was still absent. Grasp of both hands was weak, more on the right side than on the left. Both legs were weak, and the patient was unable to stand.

Obviously, some explanation of the abolition of tremor in this and similar cases other than diaschisis of the lower motor neuron is required. In discussing the abolition of parkinsonian tremor by the development of a hemiplegia, Wilson further stated:

> A fair number of cases are on record of the disappearance of tremor after an ictus of a hemiplegic kind, but it is important to note the absence of the tremor corresponds only to the time during which by diaschisis the *lower* motor neurones are functionally out of action; with some restitution of their proper activity, though the hemiplegia remains the tremor will reappear.

Unfortunately, this is not a correct statement of the facts. Not only do the observations in his own case, previously cited, completely disagree with it, but so do those in the cases of hemiplegias occurring with parkinsonism recorded in the original essay by Parkinson and in the paper by Patrick and Levy. In Parkinson's case the tremor was absent throughout the duration of the paralysis (two weeks), and as the paralyzed state of the extremities was removed the shaking returned. Obviously, the disappearance of the function of the pyramidal tract and of the tremor occurred simultaneously, as did their recovery. The same is true of the case recorded by Patrick and Levy. If these cases establish anything, it is that the disappearance of the tremor is related to interference with the supraspinal motor mechanism and in

18. Wilson, S. A. K., and Cobb, S.: Mesencephalitis Syphilitica, J. Neurol & Psychopath. **5**:44-60, 1924.

no way to any disturbance of function of the lower motor neuron. Unfortunately, the case reported by Wilson and Cobb was complicated by too many factors to make it useful in any interpretation of the physiologic mechanism of tremor. In this case the tremor eventually disappeared from the left side as well (the hemiplegia was on the right); the patient was in a semicomatose condition, and he had not only syphilis of the mesencephalon but, apparently, tabes dorsalis as well.

The experiments of Aring and Fulton [1] clearly demonstrated that although the pyramidal tract may partake in the production of intention tremor, it alone is not responsible. It is even conceivable from their experiments that it is not part of the neural mechanism producing tremor, for these authors observed that removal of the Betz cells (area 4 of Brodmann was extirpated) diminished but did not abolish tremor. It is possible that this reduction was due to the diminution in voluntary movement which was the result of this lesion or to destruction of part of the parapyramidal system which arises here. Both the results of experiments of Aring and Fulton on subhuman primates and those obtained in the human case described here are in full agreement that intention tremor is abolished when areas 4 and 6 are both extirpated. In the case reported here the evidence goes even further, for this procedure also abolished tremor at rest.

Removal of areas 4 and 6 destroys the pyramidal tract and the parapyramidal motor systems (the efferent fiber systems arising from the cerebral cortex of both area 4 and area 6 and descending to the substantia nigra, pons and other parts, which have recently been described by Levin).[19] Whether tremor is abolished because the entire efferent projection of the precentral region (both the pyramidal and the parapyramidal systems) is destroyed or merely because the parapyramidal system is completely abolished cannot at present be stated, but it is certain from the work of Aring and Fulton that complete destruction of the pyramidal tract (removal of area 4) or partial destruction of the parapyramidal systems (removal of area 6) is not sufficient to abolish intention tremor arising as a result of cerebellar lesions. These observations on both animals and man leave little doubt that the precentral cortex is an essential part of the neural mechanism which produces tremor, for, as Wilson [16] stated:

> If after development of tremor, chorea or athetosis a destructive lesion leads to cessation of involuntary movement, then that lesion must be so situated as to interrupt the neural mechanism that has been producing the movement.

19. Levin, P. M.: The Efferent Fibers of the Frontal Lobe of the Monkey (Macaca Mulatta), J. Comp. Neurol. **63**:369-419, 1936.

Recent experiments by Dusser de Barenne and McCulloch [20] may explain why in the experiments of Aring and Fulton [1] removal of area 6 alone enhanced the intention tremor engendered by cerebellar lesions. Dusser de Barenne and McCulloch demonstrated that if the activity of the narrow transitional area between area 4 and area 6 (which is sometimes called the "strip" and which they called 4-s) is increased by strychninization, the spontaneous electrical activity of area 4 is suppressed. Presumably, if the inhibitory influence of this strip on area 4 were removed by destroying strip 4-s the activity of area 4 would be increased. As it appears certain that at least part of the mechanism concerned with production of the intention tremor lies in area 4 and that the destruction of area 6 as performed by Aring and Fulton would include or seriously damage strip 4-s, it is not surprising that this procedure, in animals with intention tremor resulting from a cerebellar lesion, enhances the tremor. It will be interesting to learn whether more anteriorly placed lesions which unquestionably spare strip 4-s result in any increase in the tremor.

*Effect of Barbiturates.*—In a previous report [4] we noted that involuntary movements of another type (athetosis) were abolished not only during the period of sleep induced by these drugs but for several hours after awakening when large doses had been used. In the present case the tremor was abolished only during sleep and returned on awakening, although at times it was somewhat diminished in intensity for a short period. In the previous paper we stated:

> It is apparent . . . that the barbiturates depress either the premotor cortex (area 6) and its projection system (the parapyramidal fibers) or the subcortical centers which transmit the impulses from area 6 to a much greater extent than they depress the pyramidal system and its related cortex, area 4.

Neither on that occasion nor in the present study did we have any evidence as to whether it is the cortex and its efferent projection system or the subcortical relay centers that are depressed. It is of interest, however, that Bremer [21] recently adduced evidence which in his opinion indicates that the effect of the barbiturates is predominantly on the intercalary neurons within the cerebral cortex.

The observation previously made and cited that the barbiturates have a more profound effect on the excitability of area 6 than on that of area 4 is of interest here. From previously cited evidence,[14] we

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20. Dusser de Barenne, J. G., and McCulloch, W. S.: Functional Organization in the Sensory Cortex of the Monkey (Macaca Mulatta), J. Neurophysiol. **1**:69-85, 1938.

21. Bremer, F.: L'activité cérébrale au cours du sommeil et da la narcose: Contribution à l'étude du mécanisme du sommeil, Bull. Acad. roy. de méd. de Belgique **2**:68-86, 1937.

believe that "the involuntary movements of athetosis are projected largely from area 6"; in athetosis, moreover, the involuntary movements are abolished at times for hours after the patient awakens from the sleep produced by large doses. In experiments on intention tremor, on the other hand, Aring and Fulton [1] presented definite evidence that areas 4 and 6 are both concerned in the production of the tremor. And in our case the involuntary movement was abolished only during the period of maximum effect from the drug. With partial recovery from the drug and the relatively greater excitability of area 4 as compared with that of area 6, the tremor immediately returns, whereas athetosis does not. This observation lends support to the finding of Aring and Fulton that area 4 as well as area 6 is involved in the production of intention tremor and may well indicate that the pyramidal tract as well as the parapyramidal systems is concerned.

Recently, Putnam [22] stated that in his experience large doses of barbiturates do not abolish the movements of athetosis. This complete disagreement with our experience has concerned us. However, with a recent personal communication from Dr. Putnam, the apparent discrepancy has been removed. He stated:

> I have used pentobarbital sodium and avertin in amylene hydrate in ordinary anesthetic doses, that is, from 0.5 to 0.7 Gm. of pentobarbital sodium as a whole dose or 100 mg. of avertin per kilogram of body weight, as a routine for operation. Even with this dose the patients squirm so, especially when any sensory stimulus is inflicted, that I often have to give them ether. To be sure, while lying at rest after the operation, they are almost free from movements for twelve hours, but are usually fast asleep during this time.

Obviously, Dr. Putnam and we are talking of different circumstances. We have never stated that pentobarbital sodium in the doses we have used (0.45 Gm.) would abolish all movement when the patient was subjected to the intense sensory stimuli of a surgical operation, such as laminectomy. We were discussing the effect of the barbiturates on the involuntary movements, the situation not being confused by the presence of severe and unusual external stimuli. Dr. Putnam's last statement that the patients are almost free from movement for as long as twelve hours while lying at rest after operation is essentially in accord with our observations, though ours were not made postoperatively.

*Hemiplegia and Recovery.*—That a right hemiplegia and motor aphasia developed after removal of the precentral representation for the right upper extremity is not surprising. The motor aphasia and paralysis of the face and the lower extremity were all of short duration and were in all probability due to edema and vascular disturbance. The paralysis of the arm was more severe, but did not remain complete. That some

22. Putnam, T. J., in discussion on Bucy and Case.[4]

recovery would occur after this operation was hoped for in the light of Sachs'[23] experience. It will be recalled that Sachs had observed considerable recovery from the complete paralysis of the arm which resulted from removal of the "arm" area of the precentral gyrus. In case 3 in his series complete paralysis followed the second operation. After four weeks the patient was able to move his arm, first at the shoulder. A month later movement of the arm had further improved, and he was able to move the fingers. In case 4 there was "slight motor speech disturbance" for a few days, and by the fifteenth day after the operation the patient "had begun to move her arm quite well." In case 10 complete paralysis of the arm followed the operation. Twenty-four days after the operation "flexor movements of the fingers and elbow were first obtained." Although further improvement occurred, the extremity was never normal.

Experimentation on subhuman primates leaves little doubt that all voluntary movements originate from the precentral cerebral cortex, for when this area is completely removed from both hemispheres the animal (monkey) is completely and permanently paralyzed.[24] In the monkey, at least, removal of the precentral cortex from one hemisphere does not give rise to such a severe picture, even contralaterally, except temporarily. Thus, the precentral region of one side is capable of integrating movement in the extremities of both sides. In man this is true to a much slighter degree. In the cases reported by Gardner[25] and Dandy[26] in which the greater part of the cerebral cortex of one hemisphere, including all the precentral region, had been removed, some movement returned to the lower extremity, but the upper extremity remained completely paralyzed. It is obvious, therefore, that in man, unlike the monkey, the amount of ipsilateral cortical innervation of the upper extremity is trivial or nonexistent. Accordingly, it must be concluded that in this case and in those reported by Sachs the voluntary movement which returned to the arm after removal of the precentral arm area (areas 4 and 6) must have originated in the remaining cortex of the contralateral or damaged hemisphere. Accordingly, it is believed that this movement is the result of innervation from the parapyramidal

23. Sachs, E.: The Subpial Resection of the Cortex in the Treatment of Jacksonian Epilepsy (Horsley Operation) with Observations on Areas 4 and 6, Brain **58**:492-503, 1935.

24. Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318-342, 1933.

25. Gardner, W. J.: Removal of the Right Cerebral Hemisphere for Infiltrating Glioma: Report of a Case, J. A. M. A. **101**:823-825 (Sept. 9) 1933.

26. Dandy, W. E.: Removal of Right Cerebral Hemisphere for Certain Tumors with Hemiplegia: Preliminary Report, J. A. M. A. **90**:823-825 (March 17) 1928; Physiological Studies Following Extirpation of the Right Cerebral Hemisphere in Man, Bull. Johns Hopkins Hosp. **53**:31-51, 1933.

(and possibly the pyramidal) systems of areas 4 and 6 of the remaining "leg" and "face" areas of the hemisphere opposite the involved extremity.

That the paresis was spastic with augmentation of the tendon reflexes was to be anticipated and is in accord with the experimental results in animals (monkeys, chimpanzees and others) in which spastic paralysis followed combined removal of areas 4 and 6.[27] However, that the spasticity and hyperreflexia appeared immediately after the operation and continued thereafter is, in the light of recent investigations, a matter of some interest. Fulton and McCouch[28] have shown in subhuman primates that if the precentral region is removed some time prior to transection of the spinal cord the characteristic flaccidity and areflexia do not appear or are of much shorter duration in the contralateral extremities than in the extremities the contralateral precentral innervation of which remains intact. In this patient a similar, but not identical, situation obtained. Here, either the precentral region or its efferent projection systems had been injured about sixteen months prior to extirpation of the precentral "arm" area. This injury, incomplete as it was, had resulted in a hemiparesis and partial expressive aphasia. When the precentral arm area was removed, spastic paralysis immediately appeared, instead of the flaccid paralysis with hyporeflexia which is characteristic of sudden interference with the cortical motor systems, as in cases of ordinary apoplexy. In experiments on animals damage to the cortical motor systems some time prior to spinal transection so conditions the lower spinal centers that they take up their state of hyperreflexia sooner than they would if the cortical motor systems were intact. In the present case it seems probable that a similar process was operative, the partial damage to the precentral efferent projections having so conditioned the spinal centers that after ablation of the precentral cortex a state of spasticity and hyperreflexia developed without the usual intervening period of "shock." The Babinski sign, which was present immediately after operation and somewhat later was difficult or impossible to obtain, is to be attributed to temporary disturbances of the pyramidal tract arising from the "leg" area of area 4.

*Changes in Surface Temperature.*—The changes in surface temperature which occurred in this patient after operation (table), although slight, are, we believe, significant in the light of other observations. It will be recalled that prior to operation the surface temperature on the affected side tended to be slightly (from 0.1 to 0.8 C., or from 0.2 to

27. Fulton, J. F., and Kennard, M. A.: A Study of Flaccid and Spastic Paralyses Produced by Lesions of the Cerebral Cortex in Primates, A. Research Nerv. & Ment. Dis., Proc. **13**:158-210, 1934.

28. Fulton, J. F., and McCouch, G. P.: The Relation of the Motor Area of Primates to the Hyporeflexia ("Spinal Shock") of Spinal Transection, J. Nerv. & Ment. Dis. **86**:125-146, 1937.

1.4 F.) higher in both extremities. When the temperature was measured about five hours after operation the upper extremity was distinctly (from 0.3 to 1.9 C., or 0.45 to 3.42 F.) colder on the involved side. The lower extremities, however, showed no change from their preoperative state, either at this time or subsequently. By the next morning, approximately twenty hours after the operation, the change in the surface temperature of the upper extremity, though in the same direction, was less marked. The difference between the two sides varied from 0.1 to 0.4 C., or from 0.18 to 0.72 F. Ten hours later (i. e., about twenty-nine hours after the operation) the change was in the other direction, and the involved right arm was warmer than the left by from 0.5 to 1.3 C. (0.9 to 2.34 F.), or approximately as before operation. About a month later the findings were again comparable with those obtained before operation. The maximum fall in temperature of the right arm from the level recorded before to that obtaining shortly after operation (the room temperature being practically the same) varied from 0.4 to 2.7 C. (0.72 to 4.72 F.). At no time were there observed any differences in pulse or blood pressure on the two sides.

These observations are in agreement with those made by Kennard [29] in subhuman primates from which the entire premotor region (area 6) or motor and premotor regions (areas 4 and 6) had been removed. In those experiments, in which there was a relatively far more extensive extirpation than was made in this human case, "the temperature of the skin of the contralateral foot was found to be from 2 to 12 F. lower than that of the normal side. This change persisted in the chimpanzees for from three to six months and in the monkeys for from two to three weeks." It is believed that the changes in the case reported here were less marked and less prolonged than those in Kennard's animals because the extirpation was much less extensive.

One of us (P. C. B) reported a case [30] in which a capsular hemiplegia was associated with marked coldness and cyanosis of the involved extremities and absence of the pulse. The blood pressure could not be obtained on that side. These changes persisted for approximately four days. Unfortunately, although the surface temperature was unquestionably markedly reduced during this time, it was not accurately measured until six days after the hemiplegia developed, at which time it had returned to normal levels.

It is obvious that these observations on surface temperature could be interpreted as indicating either a failure of active vasodilatation or an overly active vasoconstriction. Kennard concluded from her observations

29. Kennard, M. A.: Vasomotor Disturbances Resulting from Cortical Lesions, Arch. Neurol. & Psychiat. **33**:537-545 (March) 1935.

30. Bucy, P. C.: Vasomotor Changes Associated with Paralysis of Cerebral Origin, Arch. Neurol. & Psychiat. **33**:30-52 (Jan.) 1935.

that it is not possible to choose between these two explanations. Our experience in the previous human case led us to conclude that in that instance the changes were due to the functional interruption of inhibitory fibers from the cerebral cortex to the vasoconstrictor mechanism, resulting in overactivity of this mechanism. Although the present case does not provide sufficient information to indicate whether the vasodilator or the vasoconstrictor mechanism was affected, it leaves little doubt that Kennard's conclusion that the premotor area (area 6) exercises some control over the vasomotor mechanism in monkeys and chimpanzees is also true for man.

SUMMARY

A man aged 33 years, after a severe cerebral injury, had a mild right hemiparesis, a slight expressive aphasia with considerable slurring of speech and a coarse unilateral tremor present both at rest and in association with voluntary muscular activity, which was marked in the right upper extremity and slight in the right lower extremity. Scopolamine hydrobromide, phenobarbital and bulbocapnine failed to influence the tremor. Soporific doses of other barbiturates abolished the tremor only during the period of sleep. The patient was operated on, and the "arm" area of the precentral region (areas 4 and 6 of Brodmann) was decorticated. After the operation the following observations were made:

1. There developed a complete right hemiplegia. The paralysis of the face and lower extremity soon largely disappeared. The paralysis of the upper extremity improved, but the movements remained slow and awkward and discrete fine movements of the hand and fingers did not return.

2. A complete motor aphasia appeared and began to subside on the eleventh day after operation, and speech soon returned to its preoperative level.

3. The tremor both at rest and on voluntary movement completely disappeared and was still absent at the time of the last report, almost fifteen months after the operation. This fact was adequately documented by electromyographic studies, by studies of the tremor with a photoelectric cell and by motion pictures.

4. The surface temperature of the right arm was lower than its preoperative level by as much as from 0.4 to 2.7 C. (0.7 to 4.9 F.) for about twenty-four hours after the operation.

From a study of these observations it is concluded:

1. An essential part of the mechanism for the production of tremor, both at rest and on voluntary movement, lies in the precentral region, i. e., areas 4 and 6 of Brodmann. Whether tremor is mediated by the parapyramidal (precentral extrapyramidal) fiber systems alone or by

the parapyramidal and pyramidal fiber systems together cannot be stated. Certainly, experimental data have demonstrated that the pyramidal system alone is not responsible.

2. The remaining precentral region, i. e., the "leg" and "face" areas of the same hemisphere, is capable of integrating considerable crude and rather awkward movement in the upper extremity after the precentral "arm" area has been removed. Fine, well coordinated movements, however, are abolished.

3. The precentral region exercises a certain degree of control over the vasomotor mechanism, since removal of the "arm" area of areas 4 and 6 results in temporary lowering of the surface temperature of the contralateral upper extremity.

4. No conclusions are drawn and no observations made relative to the nature or location of the pathologic lesion or lesions responsible for the development of the tremor in this case.

# PICROTOXIN AS A CONVULSANT IN TREATMENT OF CERTAIN MENTAL ILLNESSES

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The terror experienced by patients after an intravenous injection of metrazol was an incentive to search for another convulsant which, while sharing the benefits of metrazol (therapeutic potency and lack of serious complications), would eliminate its frightening effect. Dr. R. F. Rice, medical director of Eli Lilly & Company, Indianapolis, suggested the trial of picrotoxin and had the drug tested by animal experimentation for the latitude of its convulsive and lethal effects. Dr. K. K. Chen, who performed the experiments, reported: "The minimal convulsive dose by different routes of injection varied from one half to one third of the minimal lethal dose, a fact which points to comparative safety. A safety measure is also provided in sodium amytal, for when given intravenously it is capable of counteracting the effect of picrotoxin."

In March 1938, 3 deteriorated schizophrenic patients were selected for treatment. By the end of April 1938, a total of almost sixty convulsions had been produced without noticeable complications. This seemed to establish the relative harmlessness of the convulsant and encouraged continuance. At the time of this report (Oct. 15, 1938) 38 patients have completed one course of treatment. The illness of 19 of these patients was classified as schizophrenia, that of 8 as manic-depressive psychosis and that of 7 as belonging to a somewhat vague group of psychoses associated with psychopathic personality, mental deficiency or metabolic disturbances; 4 patients were "without psychosis," but presented disturbances of behavior sufficiently severe to warrant commitment.

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From the Psychiatric Institute (H. Douglas Singer, Director) of the Research and Educational Hospital, the University of Illinois College of Medicine.

### DOSE AND TECHNIC OF ADMINISTRATION

The picrotoxin[1] was furnished in 5 cc. ampules, each cubic centimeter containing 3 mg. of the drug. The injection was given intravenously, three times a week. Since with picrotoxin speed of injection is not required, a 22 gage needle was used. We gave as an initial dose 4 cc., regardless of the weight and age of the patient. If the dose proved to be subconvulsive, it was increased on subsequent treatment days by 1 cc. until a convulsion resulted. The largest dose averaged 8.6 cc. and ranged from 7 to 11 cc. The total dose averaged 126.3 cc. and ranged from 51 to 221 cc. The greatest number of injections given one patient was twenty-nine, and the smallest nine, with an average of seventeen and seven-tenths.

### SEX, AGE AND DURATION OF DISEASE PRIOR TO ADMISSION

The group of patients consisted of 14 men and 24 women (table 1). The average age of 27.9 years for the schizophrenic patients is relatively high for persons with this disease. The average duration of the schizophrenic illness prior to admission was thirty and six-tenths months. Hence, it is obvious that the

TABLE 1.—*Distribution According to Sex, Age, Duration of Disease and Results of Treatment of Thirty-Eight Patients*

| | Number of Patients | | Age on Admission, Years | Duration of Disease Prior to Admission, Months | Results of Treatment: Full Recoveries | | Social Recoveries | | Unrecovered Patients | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Men | Women | | | No. | % | No. | % | No. | % |
| Schizophrenias | 7 | 12 | 27.9 | 30.6 | 5 | 26.3 | .. | .... | 14 | 73.7 |
| Manic-depressive psychoses | 2 | 6 | 33.0 | .... | 5 | 62.5 | .. | .... | 3 | 37.5 |
| Other psychoses | 3 | 4 | 23.6 | 17.8 | 4 | 57.1 | 1 | 14.3 | 2 | 28.6 |
| Patients without psychosis | 2 | 2 | 34.3 | .... | 2 | 50.0 | 1 | 25.0 | 1 | 25.0 |
| Totals | 14 | 24 | 28.8 | .... | 16 | 42.2 | 2 | 5.2 | 20 | 52.6 |

patients with schizophrenia constituted a therapeutically unfavorable group. The disease had lasted more than ten years in 2 patients, more than five years in 4 and more than one year in 4; in 9 of the 19 patients it had lasted less than one year.

### RATES OF RECOVERY

Considering the small series and the short period of follow-up observation, no valid inference is possible concerning the efficacy of the treatment. However, the fact that of 19 schizophrenic patients, with a long average duration of the disease, 5 made a full recovery, suggests a promising therapeutic outlook for the picrotoxin method of shock treatment. As with metrazol medication, the manic-depressive attack was cut short with relative promptness, and severe psychoneuroses responded satisfactorily. Of the total of 18 fully or socially recovered patients, 3 have maintained their health for five months, 7 for four months, 3 for three months and 5 for less than three months; none has

1. Picrotoxin was furnished by Eli Lilly & Company.

relapsed to date. The criteria used for indicating full and social recoveries were those outlined in the report on metrazol shock treatment.[2]

### CONVULSIVE THRESHOLD

Sixteen patients had the first convulsion after the first injection; 6 of them recovered; 10 were not influenced. Five patients responded after the second injection; 2 of them recovered. Of the remaining 17 patients who responded after the third, fourth or fifth injection, 10 recovered. In other words, the patients who subsequently recovered did not have a lower convulsive threshold. The reverse rather was true. This is in accord with findings at this clinic with metrazol shock treatment,[2] but is contrary to the claims of Meduna [3] and Angyal and Gyarfas.[4]

Picrotoxin affords a measure of the convulsive threshold which is not presented by metrazol. This measure is the occurrence of repeated convulsions. It may be assumed that patients who tend to respond with repeated paroxysms in response to one injection have a lower threshold than those who react with one paroxysm only. Of the 38 patients, 2 never responded with multiple convulsions; 1 of them recovered. Of the remaining 36 patients, the group who recovered (17 patients) had an aggregate of thirty-four days with two convulsions, three days with three convulsions and one day with four convulsions, while the group who did not recover (19 patients) had an aggregate of seventy-one days with two convulsions, nine days with three convulsions and five days with four convulsions. Obviously, measured by the standard of multiple convulsions, the tendency to recover is in inverse proportion to a low convulsive threshold.

There was always an interval between the injection and the convulsion, lasting between five and forty minutes, the average being about twenty minutes. After we made the observation that when two or more convulsions occurred the $p_H$ of the blood tended to fall progressively with each successive paroxysm, in 1 instance to 6.88, we adopted the policy of giving an intramuscular injection of seconal [5]

2. Low, A. A.; Sonenthal, I. R.; Blaurock, M. F.; Kaplan, M., and Sherman, I.: Metrazol Shock Treatment of the "Functional" Psychoses, Arch. Neurol. & Psychiat. **39**:717 (April) 1938.

3. von Meduna, L.: Versuche über die biologische Beeinflussung des Ablaufes der Schizophrenie: Campher- und Cardiazolkrämpfe, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:235, 1935.

4. von Angyal, L., and Gyarfas, K.: Ueber die Kardiazolkrampfbehandlung der Schizophrenie, Arch. f. Psychiat. **106**:1, 1936.

5. Seconal (sodium propylmethylcarbinylallyl barbiturate) was supplied by Eli Lilly & Company, Indianapolis.

immediatley after the second convulsion. No third or fourth convulsion has occurred since. If two or more convulsions occurred, the interval between the injection and the first convulsion was, as a rule, shortened to from five to fifteen minutes, with an average of about nine minutes. The interval permits a study of the gradual development of the paroxysm.

### PHYSIOLOGIC OBSERVATIONS

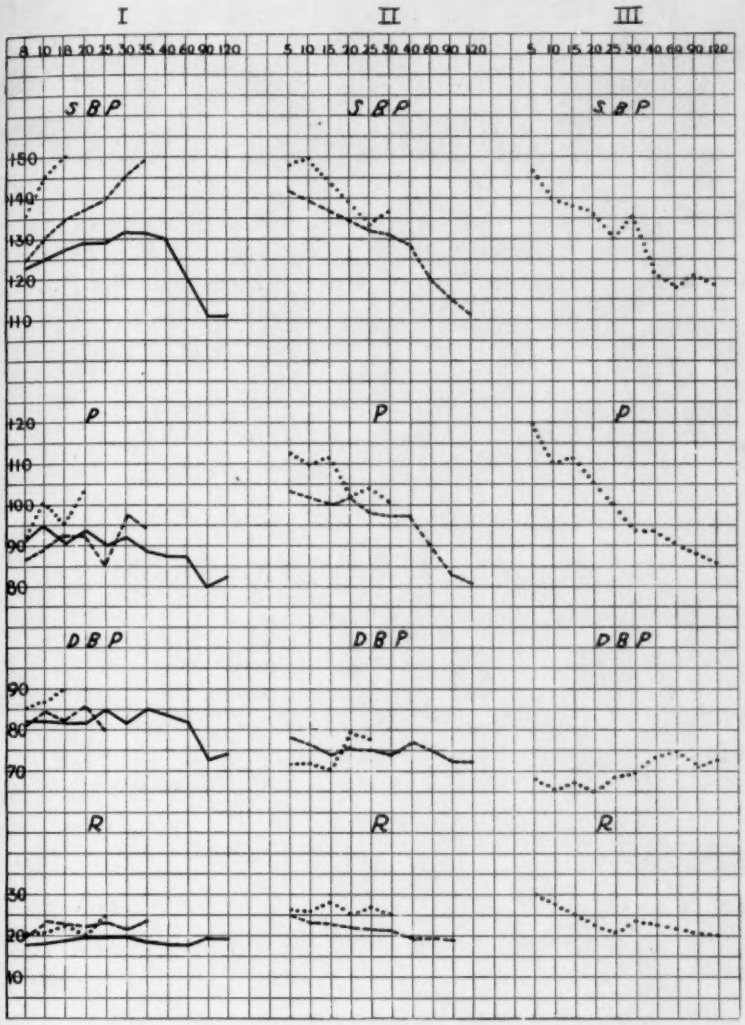
1. *Vital Signs.*—In the chart are plotted the changes in systolic blood pressure (*SBP*), pulse rate (*P*), diastolic blood pressure (*DBP*) and respiratory rate (*R*). The first column (*I*) records the changes observed after the injection and prior to the first convulsion; the second column (*II*), those after the first convulsion, and the third (*III*), those after the second convulsion. The solid line represents a group of 19 patients who on the days of recording did not have a convulsion; the broken line refers to 12 patients with one convulsion only, and the dotted line, to 7 patients who had two or more convulsions. The chart demonstrates that if no convulsion took place the blood pressure, pulse rate and respiratory rate rose moderately for about thirty-five minutes (solid line); if one convulsion was produced the values rose considerably until the convulsion began; the highest values were obtained in the first fifteen minutes after the injection if two or more convulsions developed. This indicates that the probability of the production of convulsions by the injection and the relative number of convulsions to be expected can be estimated from the rise of the curves during the first fifteen minutes after the injection.

Columns *II* and *III* show that in both the group of patients with one convulsion and that with two or more convulsions the systolic blood pressure, pulse rate and respiratory rate fell progressively soon after the convulsion, reaching an average level after about two hours. The diastolic blood pressure manifested little change.

After the second convulsion (column *III*) the systolic blood pressure, pulse rate and respiratory rate again fell progressively, while the diastolic blood pressure, after an initial fall, rose until the end of two hours.

2. *Changes in the Blood.*—Table 2 gives the means of the $p_H$, the carbon dioxide content, the calcium and dextrose levels and the leukocyte count before and after the injections. The standard deviations are not given, because of the relatively small number of observations. Eight observations were made on patients without convulsion, 9 on patients who had one convulsion only and 6 on patients during two or more consecutive convulsions. Of the last 6 patients, 2 had two con-

vulsions, 3 had three convulsions and 1 had four convulsions. In order to secure comparability with the studies made on the group of patients treated with metrazol,[2] the same methods were used: that of Stadie and




Mean values for systolic and diastolic blood pressures and pulse and respiratory rates before and after paroxysms induced by picrotoxin. The figures along the abscissas represent the number of minutes before the first paroxysm (column *I*), after the first paroxysm (column *II*) and after the second paroxysm (column *III*).

In this chart, a solid line indicates the number of patients with no convulsions; a broken line, the number with one convulsion, and a dotted line, the number with two or more convulsions.

TABLE 2.—*Means for the $p_H$, Carbon Dioxide, Dextrose, Calcium and Leukocyte Values Before and After Paroxysms*

| | No Convulsion (8 Observations) | | One Convulsion Only (9 Observations) | | Two or More Convulsions (6 Observations) | |
|---|---|---|---|---|---|---|
| $p_H$ | Fasting | 7.37 | Fasting | 7.41 | Fasting | 7.39 |
| | 10 min. after injection | 7.45 | 10 min. after convulsion | 7.13 | 10 min. after 1st convulsion. | 7.17 |
| | 20 min. after injection | 7.46 | 1 hr. after convulsion.. | 7.36 | 10 min. after 2d convulsion.. | 7.03 |
| | 30 min. after injection | 7.35 | 2 hr. after convulsion.. | 7.43 | 10 min. after 3d convulsion.. | 6.97 |
| | 90 min. after injection | 7.44 | | | 10 min. after 4th convulsion. | 6.88 |
| | 150 min. after injection | 7.42 | | | 1 hr. after last convulsion.. | 7.27 |
| Carbon dioxide, volume per cent | Fasting | 58.8 | Fasting | 58.0 | Fasting | 57.7 |
| | 10 min. after injection | 60.0 | 10 min. after convulsion | 31.8 | 10 min. after 1st convulsion. | 30.7 |
| | 20 min. after injection | 61.5 | 1 hr. after convulsion.. | 48.2 | 10 min. after 2d convulsion.. | 18.8 |
| | 30 min. after injection | 53.7 | 2 hr. after convulsion.. | 57.9 | 10 min. after 3d convulsion.. | 14.5 |
| | 90 min. after injection | 54.7 | | | 10 min. after 4th convulsion. | 9.0 |
| | 150 min. after injection | 57.8 | | | 1 hr. after last convulsion.. | 30.3 |
| Calcium, mg. per 100 cc | Fasting | 9.76 | Fasting | 9.32 | Fasting | 10.3 |
| | 10 min. after injection | 10.00 | 10 min. after convulsion | 9.67 | 10 min. after 1st convulsion. | 10.6 |
| | 20 min. after injection | 9.80 | 1 hr. after convulsion.. | 9.44 | 10 min. after 2d convulsion.. | 10.9 |
| | 30 min. after injection | 10.00 | 2 hr. after convulsion.. | 9.42 | 10 min. after 3d convulsion.. | 10.9 |
| | 90 min. after injection | 10.00 | | | 10 min. after 4th convulsion. | 11.5 |
| | 150 min. after injection | 9.85 | | | 1 hr. after last convulsion.. | 10.4 |
| Dextrose, mg. per 100 cc | Fasting | 89.9 | Fasting | 85.1 | Fasting | 90.4 |
| | 10 min. after injection | 86.8 | 10 min. after convulsion | 122.5 | 10 min. after 1st convulsion. | 136.4 |
| | 20 min. after injection | 75.2 | 1 hr. after convulsion.. | 118.0 | 10 min. after 2d convulsion.. | 160.2 |
| | 30 min. after injection | 108.5 | 2 hr. after convulsion.. | 100.8 | 10 min. after 3d convulsion.. | 181.2 |
| | 90 min. after injection | 106.6 | | | 10 min. after 4th convulsion. | 210.4 |
| | 150 min. after injection | 100.3 | | | 1 hr. after last convulsion.. | 146.3 |
| White blood corpuscles per cu. mm. | Fasting | 9.780 | Fasting | 8.560 | Fasting | 10.660 |
| | 10 min. after injection | 10.860 | 10 min. after convulsion | 15.020 | 10 min. after 1st convulsion. | 18.880 |
| | 20 min. after injection | 10.920 | 1 hr. after convulsion.. | 10.530 | 10 min. after 2d convulsion.. | 22.600 |
| | 30 min. after injection | 13.290 | 2 hr. after convulsion.. | 11.780 | 10 min. after 2d convulsion.. | 27.600 |
| | 90 min. after injection | 10.210 | | | 10 min. after 4th convulsion. | 34.300 |
| | 150 min. after injection | 9.275 | | | 1 hr. after last convulsion.. | 22.030 |
| Polymorphonuclears, percentage | Fasting | 69.0 | Fasting | 62.1 | Fasting | 63.2 |
| | 10 min. after injection | 67.8 | 10 min. after convulsion | 49.8 | 10 min. after 1st convulsion. | 49.8 |
| | 20 min. after injection | 72.3 | 1 hr. after convulsion.. | 70.7 | 10 min. after 2d convulsion.. | 43.7 |
| | 30 min. after injection | 70.5 | 2 hr. after convulsion.. | 83.6 | 10 min. after 3d convulsion.. | 45.2 |
| | 90 min. after injection | 74.0 | | | 10 min. after 4th convulsion. | 28.0 |
| | 150 min. after injection | 79.7 | | | 1 hr. after last convulsion.. | 83.5 |

Van Slyke [6] for carbon dioxide content, the Somogyi modification of the Shaffer and Hartman method [7] for dextrose and the Kramer-Tisdall method [8] for total calcium. In order to save time, the simple procedure with the Malcolm Dale glass electrode was used for determination of the $p_H$; the method has been found by various authors to give satisfactory results.[9]

Table 2 shows that in observations made on patients without convulsions there was no significant difference between the sample taken during fasting and those obtained at various intervals after the injection. The leukocyte count alone exhibited a moderate rise thirty minutes after the injection.

In patients who had a single convulsion the $p_H$ and the carbon dioxide content fell considerably ten minutes after the injection and recovered after one hour. The calcium and dextrose remained relatively stationary; the leukocyte count rose, and the polymorphonuclear cells decreased significantly. These changes are practically the same as those encountered in patients treated with metrazol.

The changes were more intense in the group of patients in whom two or more convulsions were recorded. The $p_H$ and the carbon dioxide content decreased progressively in the samples taken ten minutes after each successive convulsion, and were not restored to the fasting levels even one hour after the last convulsion. The total calcium remained stationary. The dextrose content and the number of leukocytes increased progressively ten minutes after each convulsion, the sugar value finally reaching 210.4 mg. per hundred cubic centimeters and the white cell count 34,300 after the fourth paroxysm, with the fasting levels not yet restored one hour after the last paroxysm.

Table 2 seems to indicate that, measured by chemical changes of the blood, the effect of the drug is relatively negligible as compared with that of the convulsion.

### COMPARISON OF PAROXYSMS INDUCED WITH METRAZOL AND WITH PICROTOXIN

The paroxysm induced with picrotoxin is practically identical with that produced by metrazol, both in progression and duration. It is

6. Stadie, W. C., and Van Slyke, D. D.: Carbon Dioxide Content and Capacity in Arterial and Venous Blood Plasma, J. Biol. Chem. **41**:191, 1920.

7. Somogyi, M.: A Reagent for the Copper-Iodometric Determination of Very Small Amounts of Sugar, J. Biol. Chem. **117**:771, 1937.

8. Tisdall, F. F.: A Note on the Kramer-Tisdall Method for the Determination of Calcium in Small Amounts of Serum, J. Biol. Chem. **56**:439, 1923.

9. Bayliss, L. E.; Kerridge, P. T., and Verney, R. C.: The Determination of the Hydrogen Ion Concentration of the Blood, J. Physiol. **61**:448, 1926. Harris, I.; Rubin, E. L., and Shutt, W. J.: Modifications in the Use of Glass Electrode for the Determination of the $p_H$ of Venous Blood, ibid. **81**:147, 1934. DuBois, D.: Glass Electrode for Testing the $p_H$ of Blood, Science **76**:441, 1932.

usually initiated by a cry or cough and is followed by spasmodic opening of the mouth. The seizure consists of an initial clonic phase, which lasts an average of six seconds, a tonic phase of about twelve to fourteen seconds' duration and a final clonic phase of about forty seconds' duration. The cyanosis, the flush and the postparoxysmal motor agitation are of about the same intensity and distribution as with metrazol. If successive convulsions occur the cyanosis tends to become more marked with each paroxysm.

None of the patients showed any intense fear of the treatment. Some of them had previously received a course of intravenous injections of metrazol and volunteered statements comparing the two procedures. One said: "It is easier than metrazol. Picrotoxin doesn't give you as many sensations as metrazol." Another patient remarked: "I don't like any treatments, but I'd rather take this than metrazol. It is not so strong; it doesn't make me go dizzy."

## COMPLICATIONS

Mandibular subluxation was infrequent. One patient suffered a fracture of the left scapula, two others dislocation of the shoulder. Restoration of function was prompt after orthopedic treatment. The fracture and the dislocations occurred in the early stage of our experience, when the patients were not watched with sufficient care during the interval between the injection and the convulsion. With the last 25 patients no complication was encountered.

## CONCLUSIONS

In a group of 38 patients convulsions were produced by means of intravenous injections of picrotoxin.

Because of the interval between injection and the first convulsion, on the one hand, and that between the first and subsequent convulsions, on the other, the action of both the drug and the convulsions can be conveniently studied.

Picrotoxin does not produce the terror incidental to metrazol.

The therapeutic results appear to be promising.

# MENTAL AND PHYSICAL GROWTH IN PUBERTAS PRAECOX

## REPORT OF FIFTEEN YEARS' STUDY OF A CASE

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The subject of pubescence has a vast literature, both medical and anthropologic. Recent studies of growth reflect increased attention to the physiologic aspects of normal adolescence. Abernethy [1] investigated the correlations in physical and mental growth based on a study of 487 American high school girls. She found that the average age of physiologic maturation in 48 per cent of these girls was approximately 13 years and 6 months.

Petri [2] analyzed hereditary factors in the determination of menarche by comparing 51 pairs of monozygotic twins with 47 pairs of dizygotic twins. The mean difference in the menarche in the latter group was one year. The mean difference among monozygotic pairs was only two and eight-tenths months.

Pryor [3] reported a serial study of the adolescent spurt of growth for 100 girls. Examinations extending over four years at six month intervals demonstrated that pubescent girls grew 26 per cent faster than nonpubescent girls during the six months before the appearance of menses. A predominant pattern of axillary and pubic hair accompanied the onset of catamenia, regardless of chronologic age.

Shuttleworth [4] contributed an elaborate statistical analysis of the longitudinal data derived from the Harvard Growth Studies, initiated

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1. Abernethy, E. M.: Correlations in Physical and Mental Growth, J. Educ. Psychol. **16**:458-466, 1925.

2. Petri, E.: Untersuchungen zur Erbbedingtheit der Menarche, Ztschr. f. Morphol. u. Anthropol. **33**:43-48, 1934-1935.

3. Pryor, H. B.: Certain Physical and Physiologic Aspects of Adolescent Development in Girls, J. Pediat. **8**:2-12, 1938.

4. Shuttleworth, F. K.: Sexual Maturation and the Physical Growth of Girls Six to Nineteen, Monographs of the Society for Research in Child Development, Washington, D. C., National Research Council, 1937, p. 253.

by Prof. Walter F. Dearborn in 1922. This study comprised a total of 3,650 children who were measured annually as long as they remained in school. His interpretations were based on the theory that "patterns of physical growth during the adolescent period are largely under the control of endocrine factors which presumably begin to operate at an early age in some children and at a late age in others." Such longitudinal data on normal children will be of value as a base of reference in consecutive studies of individual cases of pubertas praecox, particularly when physical measurements are available prior to the onset of pubescence.

Studies of pubertas praecox to date have been limited almost to reports of single cases, with occasional necropsy observations but with meager psychologic and developmental data. Keene and Stone [5] assembled a total of 80 cases of pubertas praecox, chiefly from American, German and English journals. Forty-seven, or almost 60 per cent, of the patients were girls. In this group of girls the symptoms made their appearance approximately as follows: at birth in 11 per cent; in the first year, 25 per cent; in the second year, 20 per cent; in the third year, 7 per cent; in the fourth year, 7 per cent, and in the fifth year, 7 per cent. In over three quarters of the cases the menarche appeared in the first five years. In a similar proportion of boys the symptoms of juvenile hypergonadism appeared in the first five years of life, with a high frequency of over 19 per cent during the age period of 30 to 36 months. In only 15 of the 80 cases were psychometric data concerning mental status available.

In the case to be reported here physical and mental measurements were made over a period of fifteen years. The case was first briefly reported by Thoms and Hershman.[6] Gesell [7] reported the same case at greater length and with special reference to the influence of pubertas praecox on mental growth. The present final report reviews all the accrued data and likewise emphasizes the developmental factors, both physical and mental.

## REPORT OF CASE

*Medical and Neurosurgical History.*—J. B.,[8] a Russian Jewess, was born on July 22, 1919. The father is alive and well at the time of this report. An older brother appears normal. The mother died of influenza in 1920. Both the mother

5. Keene, C. M., and Stone, C. P.: Mental Status as Related to Puberty Praecox, Psychol. Bull. **34**:123-133, 1937.

6. Thoms, H., and Hershman, A. A.: A Case of Sexual Precocity, Am. J. Obst. & Gynec. **6**:349, 1923.

7. Gesell, A.: (*a*) The Influence of Puberty Praecox upon Mental Growth, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1926, vol. 1, pp. 511-538; (*b*) Infancy and Human Growth, New York, The Macmillan Company, 1929, chap. 13, pp. 245-271.

8. This case has also been reported under the initials H. J. by Gesell.[7b]

and maternal grandmother had a normal menstrual history. The patient suffered no serious illnesses throughout infancy and childhood.

Dentition occurred at about 7 months, and the patient began to walk at 11 months. As early as the age of 1 year the father noticed that the breasts were unusually large. During February 1923, when the patient was 3½ years of age, she experienced menstruation, with a good amount of flow which lasted four days. Six weeks later a similar menstruation occurred, lasting three days. The next menstruation occurred three weeks later. Then followed a period of amenorrhea of eight weeks. The subsequent menstrual history will be detailed in a section devoted to that subject.

Physical examination at the time of menarche showed a well nourished, plump child with the statural configuration of a mature woman. Her height was 42 inches (106.7 cm.) and her weight 50 pounds (22.7 Kg.).

The breasts were mature; the primary areolas were well differentiated and the nipples well defined and protuberant. There was no secretion. Pubic hair was

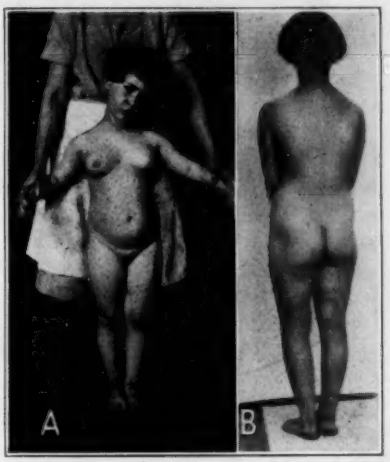


Fig. 1.—J. B.: *A*, at 3½ years, when her height was 42 inches (106.7 cm.); *B*, at 8½ years, when her height was 53.5 inches (135.9 cm.).

moderately thick and covered the pubes. Axillary hair was absent. The labia of the external genitalia were well developed. Vocal timbre was richer and deeper than average. A roentgenogram of the sella turcica was normal and showed a normal-sized cavity.

Neurologic and Neuropathologic Findings: The first suggestion of intracranial abnormality was presented in 1932, at which time the girl was referred by the school nurse because of myopia and astigmatism, for which glasses were prescribed and secured. In April 1937 she had rather severe headaches, became nauseated and experienced projectile vomiting. On May 8, 1937, she came to the ophthalmologic clinic again, complaining of an internal squint on the right; glasses were ordered and delivered. Roentgenograms of the skull at that time showed convolutional atrophy, which was believed to be within normal limits. However, she was noted to have paresis of the right external rectus muscle, papilledema of 2 or 3 diopters and retinal hemorrhages. Previous to this time the only hint of an intracerebral lesion was dull frontal headache lasting but a few minutes and coming on usually in the evening.

She was admitted to the hospital in June 1937, when she told of frontal headaches of about four weeks' duration, which were sharp and throbbing and lasted two or three hours. About the same time that the headaches became sharp, the squint on the right was becoming prominent and she was beginning to see double, particularly on looking to the right. Neurologic examination at that time showed normal cerebration, no impairment of skilled acts, no involvement of the cranial nerves and no gross defect in the visual fields.

Examination of the fundi showed both disks to be choked, with papilledema of 3 diopters. There was also definite paresis of the right external rectus muscle. There was no evidence of motor atrophy or weakness. The results of coordination tests (finger to nose, heel to toe and rapidly alternating movements) were all normal. Sensory examination gave entirely normal results. The impression at that time was that she had dyspituitarism with a superimposed expanding pituitary neoplasm. This diagnosis could not be substantiated, and it was thought by the neurosurgical service that there was a subtentorial lesion.

On June 15, 1937, the posterior fossa was explored. There was found to be some obstruction to the aqueduct of Sylvius, thought possibly due to a tumor lying on the roof of the fourth ventricle. A few bits of tissue taken for biopsy showed no evidence of tumor. Postoperatively, the patient complained of headaches for three or four weeks, which were relieved by daily lumbar puctures. Encephalograms on July 9, 1937 (three and one half weeks after operation), were indeterminate, but showed an intraventricular filling defect, possibly due to a blood clot. She continued to improve slowly and was discharged on Sept. 22, 1937.

She was observed in the neurosurgical dispensary for one month, after which time she was readmitted. At the time of readmission she had a recurrence of her symptoms, chiefly severe frontal and occipital headaches and bulging of the decompression, accompanied with nausea and vomiting. She complained of rather marked dizziness and ataxia, particularly when she lay on her back. There was nystagmus on both left and right lateral gaze, more marked on the left; no facial weakness or evidence of involvement of the sixth nerve was apparent at this time. The eyegrounds showed definite pallor and blurring of the disks, with considerable secondary atrophy. The decompression was slightly bulging but not soft. Otherwise results of examination were not remarkable. Neurologic examination was somewhat confusing, in view of findings thought to be due to the previous cerebellar exploration, during which the vermis had been split. Her gait was definitely cerebellar; she was extremely unsteady on her feet and had a tendency to fall to the left. Lumbar puncture showed an initial pressure of 290 mm. It was believed that she had a tumor of the brain, probably in the region of the aqueduct of Sylvius. A ventriculogram taken on Nov. 18, 1937, showed evidence of considerable increase in the internal hydrocephalus, compatible with block in the posterior fossa. The air could be traced down to the third ventricle and showed a block of the aqueduct, which was displaced to the right.

On November 29 reexploration of the posterior fossa showed a tumor occupying almost the entire left cerebellar hemisphere. The mass was removed in toto. The patient seemed to be extremely sensitive to any manipulation in the region of the tumor. Her blood pressure fell considerably on two occasions, and the procedure had to stop temporarily, owing to the slowing of her respiratory rate. The day following the operation the patient's vital signs rose sharply, the temperature reaching 103 F., and she complained of severe pain in the back of the neck. Lumbar puncture was done, but failed to relieve the symptoms.

On December 3 (four days postoperatively) lumbar puncture showed some thick pinkish necrotic material coming through the needle. On smear this material turned out to be pus without obvious organisms. Culture of the fluid showed a

growth of atypical-appearing nonhemolytic streptococci. Administration of sulfanilamide in a dose of 60 grains (3.88 Gm.) was started, the vital signs diminished, and the patient looked much better. Daily lumbar puncture was done, and the sulfanilamide therapy continued. The spinal fluid continued to be cloudy, and five positive cultures of the same organism were obtained. Medication with sulfanilamide

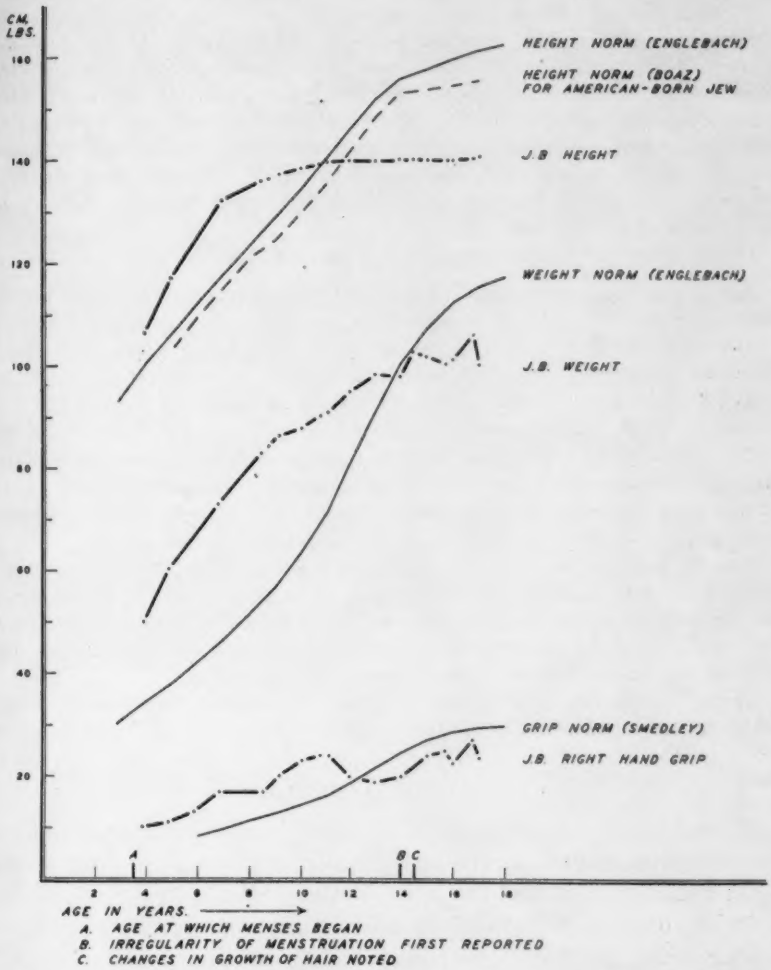


Fig. 2.—Chart of physical growth of J. B. Physical measurements are plotted against Boas, Smedley (Whipple, G. M.: Manual of Mental and Physical Tests: I. Simpler Processes, Baltimore, Warwick & York, 1914) and Engelbach (Engelbach, W.: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932, vol. 1, pp. 261-312) norms.

was continued for one month, when the level in the blood was 6.4 mg. and in the spinal fluid 4.2 mg. per hundred cubic centimeters. Her general condition became gradually worse, and she died on Jan. 5, 1938, thirty-seven days after operation. Postmortem examination was not made.

The final clinical diagnosis was tumor of the posterior fossa. The growth was described as follows by Dr. H. M. Zimmerman: "The histologic appearance of this tumor is that of typical fibrillary astrocytoma. It is not encapsulated by any connective tissue, as appeared macroscopically. Its only unusual features are the great vascularity and the large acellular zones of fibrils. The latter had the appearance of gelatinous tissue in the gross."

*Physical Growth.*—Physical examination of the head, neck, chest, abdomen and extremities revealed nothing abnormal at the age of 3½ years. At this same age, however, a roentgenogram of the wrists showed advanced development. The trapezoid bone, which usually appears between 5 and 8 years of age, was present, as was the pisiform, which usually appears between the tenth and the thirteenth year. The styloid process of the ulna, seldom seen before the eleventh year, was also present. At the age of 4 years and 8 months the pisiform bone was fully ossified, and the general maturity of the carpal bones was judged to represent an age between 12 and 14 years.

Further observations concerning physical characteristics included the following:

Age 5 Years and 11 Months: The denture was complete and almost perfect. There were no 6 year molars. Dentition was reported to have begun at 7 months. A roentgenogram of the skull at the age of 4 years and 8 months had shown the second molar to be unerupted and the first molar questionable.

Age 8 Years and 3 Months: Axillary hairs were present.

Age 14 Years and 6 Months: Several coarse brown hairs surrounded the nipples. There was a well defined male distribution of hair, consisting of a sparse line of coarse long dark brown hairs from the navel to the pubes. There was no increase in height, but a relatively marked increase in weight and in circumference of the chest. The flesh continued to be hard and firm.

Age 16 Years: The child was composed and relaxed during measurements. Many moles with dark brown pigmentation were present on the body. There was considerable lanugo on the lower part of the lumbar region of the spine. The lower parts of the legs were covered with light-colored fairly coarse hair. The flesh was less firm than at the previous examination.

Age 16 Years and 6 Months: A rather well defined light-colored downy moustache had appeared. The distribution of the remaining hair was as before.

## PELVIC MEASUREMENTS

A study of the bony pelvis in this case is of considerable interest. The data presented are the result of two roentgenologic investigations, one in February 1930 and the other in March 1937.

Before describing the findings, however, it is pertinent to speak of certain studies on the development and variations of the "normal" female basis, as shown by roentgen investigations. This interest has long been a major one in the obstetric clinic at Yale University, and numerous communications have appeared on the subject.[9] Recently we

9. Thoms, H.: The Obstetrical Significance of Pelvic Variations: A Study of Four Hundred and Fifty Primiparous Women, Brit. M. J. **2**:210, 1937; Routine Roentgen Pelvimetry in Six Hundred Primiparous White Women Consecutively Delivered at Term, Am. J. Obst. & Gynec. **37**:101, 1939.

have classified the variations of the female adult basis into four general groups, according to the shape of the superior strait, or pelvic inlet. The percentages shown in table 1 are based on consecutive measurements of 600 white women observed at the outpatient clinic, 100 white college women studied by Greulich and Thoms,[10] and 65 prepubescent girls.

It seems to us that evidence is beginning to demonstrate that the ultimate form of the adult pelvis is determined not a little by certain influences which are brought into play during the pubescent years. These influences are probably hormonal and nutritional. In the present case, in which the hormonal influence may be considered abnormal, a study of the bony pelvis with the aforementioned classification in mind is of considerable interest.

TABLE 1.—*Classification of the Variations in the Female Pelvis*

| Type | | Incidence (%) in 600 White Women at the Outpatient Clinic | Incidence (%) in 100 White College Women | Incidence (%) in 65 Prepubescent Girls |
|---|---|---|---|---|
| Dolichopellic | Anteroposterior diameter longer than transverse | 15.3 | 37.0 | 64.6 |
| Mesatipellic | Anteroposterior and transverse diameter of equal lenth or anteroposterior shorter than transverse by not more than 1 cm. | 45.3 | 46.0 | 30.8 |
| Brachypellic | Anteroposterior diameter between 1 cm. and 3 cm. shorter than transverse | 35.0 | 17.0 | 4.6 |
| Platypellic | Anteroposterior diameter shorter than transverse by 3 cm. or more | 4.3 | 0.0 | .... |

Two roentgenograms were taken in 1930, a straight line anteroposterior view of the pelvis with the patient horizontal and a lateral view with the patient in the lateral horizontal position. In the former roentgenogram the anteroposterior diameter of the pelvis seemed definitely elongated. There was well defined ossification of the epiphyses of the crests of the ilia. The spines of the pubic bones definitely encroached on the pelvic cavity, and the outlet appeared wide. In the lateral view taken at this time the sacrosciatic notch appeared exceptionally wide and rectangular, and a comparison between this view and one taken seven years later showed no essential differences.

The roentgenograms of the pelvis in 1937 were taken according to the pelvimetric technic most recently described by Thoms and Wilson.[11]

10. Greulich, W. W., and Thoms, H.: The Dimensions of the Pelvic Inlet in Seven Hundred and Eighty-Nine White Females, Anat. Rec. **72**:45, 1938.

11. Thoms, H., and Wilson, H. M.: Roentgen Methods for Routine Obstetrical Pelvimetry, Yale J. Biol. & Med. **10**:437, 1938.

By this technic all the important diameters are accurately determined, and a reduction of the outline of the superior strait to actual dimensions becomes possible. Figure 3 presents an outline of the superior strait, showing a typical dolichopellic type of inlet in 1937.

The pelvic measurements in our case follow:

| | Cm. |
|---|---|
| Anteroposterior diameter, superior strait | 12.00 |
| Transverse diameter, superior strait | 11.25 |
| Posterior sagittal diameter, superior strait | 6.00 |
| Interischial spinous diameter | 8.75 |
| Anteroposterior diameter, narrow pelvic plane | 12.00 |
| Posterior sagittal diameter, narrow pelvic plane | 5.75 |
| Bituberal diameter | 10.00 |
| Posterior sagittal diameter, outlet | 9.00 |

The lateral view taken in 1937 (fig. 4) showed the bones of the pelvis to be slight and graceful as compared with the male pelvis and the sacrosciatic notch exceptionally wide and rectangular, making the posterior part of the pelvis in the narrow plane exceptionally roomy. The increase in the posterior part of the pelvis was present from inlet to outlet, as witnessed by the posterior sagittal diameters, all of which were from 1 to 2 cm. longer than the average in the adult female pelvis.

The significance of these pelvic characteristics in a girl 18 years of age will be considered later in the section on developmental factors.

### MENSTRUAL HISTORY

Menstruation began at the age of 3 years and 7 months, and after slight initial irregularity occurred at from twenty-eight to thirty day intervals until the age of 13 years, when irregularity was first reported. This irregularity continued and increased from year to year, the periods becoming less frequent. The health and the general condition, however, appeared to be excellent until the age of 17 years and 8 months, when the patient complained of considerable pain preceding the menstrual period and of headaches, which came on suddenly and lasted variable lengths of time. These symptoms, it will be noted, occurred almost exactly fourteen years after the precocious menarche. Figure 5 summarizes the course of the menstrual history between the ages of 14 years and 8 months and 17 years and 9 months.

Dr. Ralph I. Dorfman, of the Adolescence Study Unit, assayed the urine of J. B. for estrogenic and comb-stimulating substances on Sept. 2, 1937 (when she was 18 years old). Through the courtesy of William Walter Greulich the following summary of the findings is available: A twenty-four hour sample of urine showed 31 international units of estrogenic, and 13 international units of comb-stimulating, or so-called androgenic, substance. The amount of these substances was definitely

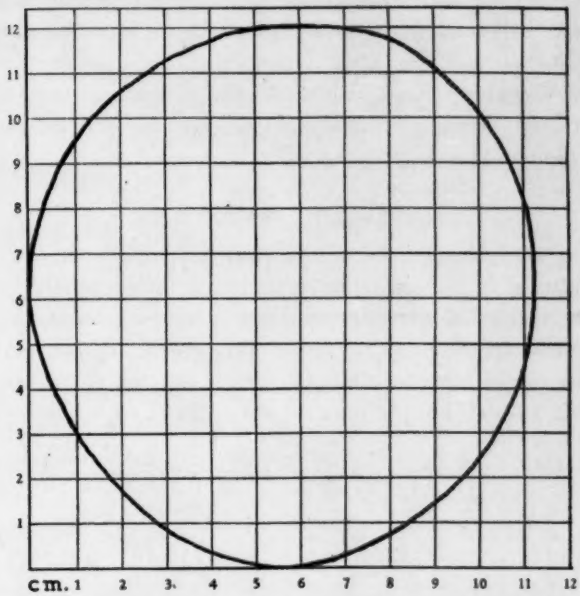


Fig. 3.—Outline of superior strait in 1937, showing typical dolichopellic type of inlet.

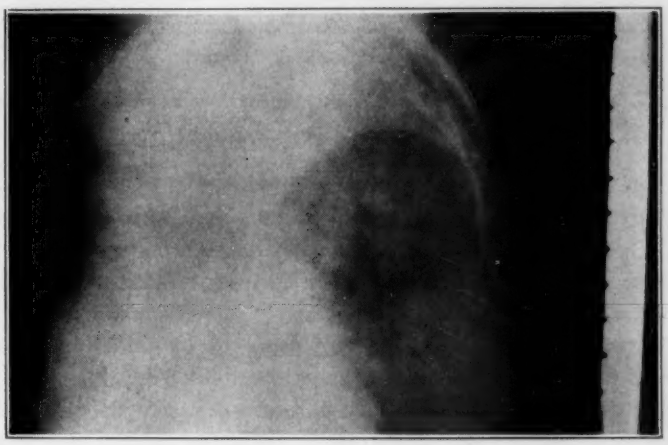

Fig. 4.—Lateral roentgenogram of the pelvis, taken in 1937. The relatively large sacrosciatic notch shows unusual room in the posterior part of the pelvis. The scale at the side represents centimeters in the sagittal plane of the body.

lower than that excreted by the normal adult woman, in whose urine from about 50 to 600 international units of estrogenic, and 20 to 50 international units of androgenic, substance are excreted in twenty-four hours.

Studies elsewhere have indicated that a marked reduction of the androgenic and estrogenic substances is characteristic of urine during and after the menopause.

## PSYCHOLOGIC DEVELOPMENT

Behavior may be regarded as the most inclusive indicator of developmental status. In the instance reported it is especially pertinent to determine the psychologic effects of the precocious onset of pubescence and of menstruation recurring regularly throughout the years of childhood. One might surmise that the course of mental growth would be considerably altered, but the data do not support such a surmise.

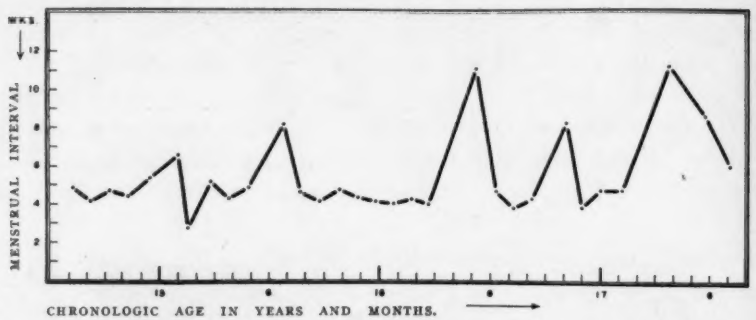


Fig. 5.—Chart showing menstrual intervals between 14 years and 6 months and 17 years and 7 months.

Fortunately, the psychologic data are abundant, a total of sixteen mental examinations and follow-up contacts having been made between the ages of 3 years 11 months and 17 years 9 months.[12] The findings for these examinations, expressed in terms of maturity, are partially summarized in figure 6. Psychometric determinations and clinical impressions as well reveal a rather surprising approximation to a normal course of mental growth. In spite of the extreme physiologic deviation, the patient made average progress through the elementary school, took high school courses in stenography and typewriting and developed normal vocational interests. She never became a problem child in conduct and during her long terminal illness at the hospital showed creditable character and stability.

12. Miss Elizabeth Evans Lord and Burton M. Castner assisted in psychologic examinations.

The main characteristics of her mental development may be most briefly and objectively summarized under the following headings: (*a*) intelligence, (*b*) motor traits and (*c*) personality.

(a) *Intelligence.*—At all times J. B. showed relatively normal memory, insight, comprehension and command of words. When measured by the Yale norms and the Stanford-Binet tests, she consistently rated at or near an average level, with an intelligence quotient ranging generally from 90 to 100.

No marked precocities or recessions of ability were noted in the various tests. She learned to write, spell and read at an ordinary rate

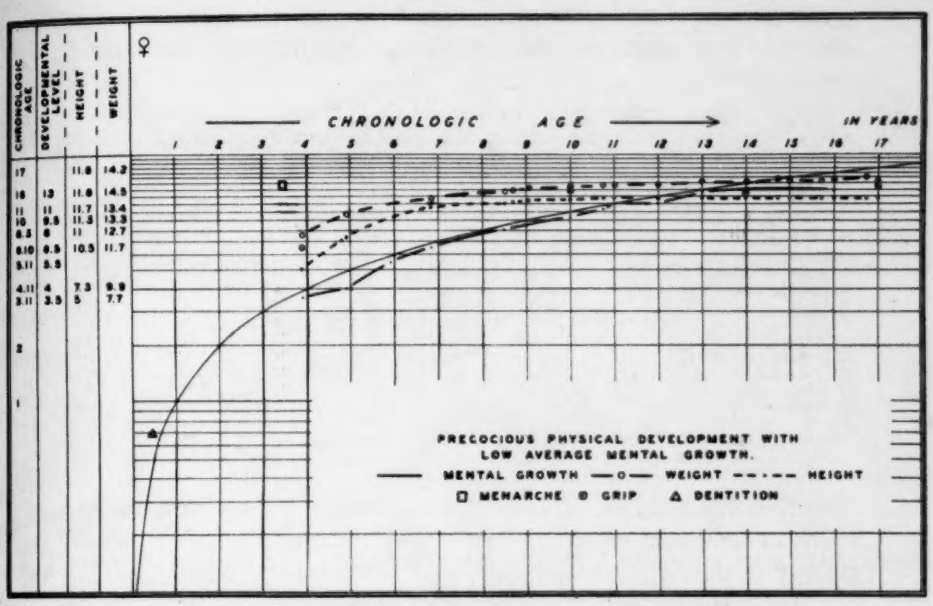


Fig. 6.—Chart of mental and physical growth of J. B.

of improvement. She read orally with moderate fluency; her interest in stories matured in a natural manner. Her vocabulary increased at a normal rate and fell only slightly below the norm for her age. She graduated from a commercial course at 17 years of age, having attained a stenographic speed of from 100 to 120 dictated words and a typing speed of 40 words per minute. Her progress through the elementary grades was steady, and the quality of her school work was average.

(b) *Motor Traits.*—In motor demeanor J. B. was rather slow and deliberate. This deliberation gave an aspect of poise to her movements in early childhood. Under the stress of play, however, she ran and

romped with other children. Her posture and carriage were excellent through the entire period of observation. The exceptional motor symptoms which occurred in association with the cerebellar tumor have been detailed in the section on medical and neurosurgical history.

There was no evidence of marked acceleration in locomotion, body control or manual motor coordination. Specimens of handwriting at the ages of 7, 8½ and 10 years (fig. 7) showed the gradations in amplitude, pencil pressure, size and precision appropriate to these ages. Similar trends showed themselves in imitative drawings of geometric figures and in the spontaneous drawings of a man.

The drawings of a man are reproduced in figure 8, because they give definite evidence of the same gradual psychomotor maturation which one finds in normal girls who are not handicapped by an exceptionally

TABLE 2.—*Developmental Ratings of J. B. (4 to 17 years)*

| | Age Level in Developmental Items, Years | | | | | | |
|---|---|---|---|---|---|---|---|
| Chronologic Age at Examinations | Imitative Drawing | Spontaneous Drawing | Vocabulary | Digit Recall | Reading | Comprehension | Developmental Level |
| 4 years | 4 | 3½ | 3½ | 4 | .. | 3½(?) | 3½ |
| 5 years | 4½ | 4 | 4 | 4 | .. | 4 | 4 |
| 6 years | 5½ | 6 | 5½ | 7 | 6 | 5½ | 5½ |
| 7 years | 7 | 6(?) | 6(?) | 10 | 7½ | 6 | 6½ |
| 8½ years | .. | .. | 7½(?) | 10 | 8 | 7 | 8 |
| 10 years | .. | .. | 8½ | 10 | 10 | 9 | 9½ |
| 10½ years | .. | .. | 8½ | 11 | 10½ | 10 | 10½ |
| 11 years | .. | .. | 8 | 12 | 11 | 11 | 11 |
| 12 years | .. | .. | 9½ | 12 | 11 | 11 | 11 |
| 13 years | .. | .. | 12 | 18 | .. | 14 | 12½ |
| 16 years | .. | .. | 14 | 14 | 12 | .. | 13 |
| 17 years | .. | .. | 15 | .. | .. | 16 | 15 |

precocious pubescence. The manner in which these drawings were executed also certified to a typical rather than an unusual personality makeup of the successive ages.

The 4 and 5 year drawings of the man were slightly below the average, but were made with the uncritical alacrity characteristic of these preschool ages. At the age of 8½ years a childlike self criticism crept into her responses. She made two efforts at drawing a suitable profile and then reversed the paper and needed encouragement from the examiner before she completed the drawing. At the age of 10 years, likewise, there were a good deal of self criticism and many erasures. It took her eleven minutes to complete the picture. At the age of 11 years there was not a single erasure, and the drawing was completed in about two minutes. The series of drawings pictured gives a fair indication of the general rate of her intellectual maturation.

(c) *Personality.*—On her first examination (at 4 years) J. B. had a restrained demeanor and spoke with a voice of rich timbre and deep tone. This subdued gravity had a thick, lethargic quality which was

unchildlike, but she gave no evidence of advanced maturity in her interests. She played with dolls and had a childlike fear of dogs.

At the age of 5 years her gravity was even more conspicuous. She seemed to be mature in her poise, sat quietly in her chair without showing the volatile attention one expects at this age. Some of this "poise" may have been due to the discipline of close association with a dominat-

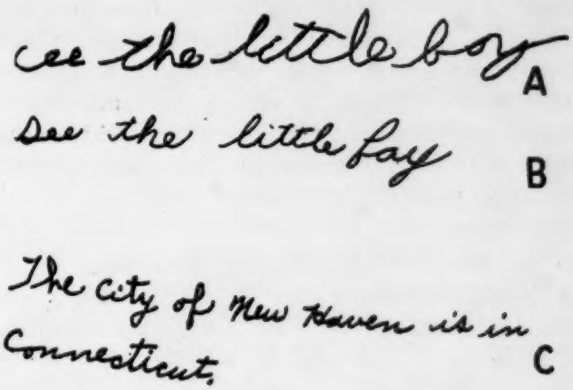


Fig. 7.—Handwriting of J. B. at 7 (*A*), 8½ (*B*) and 10 (*C*) years of age.

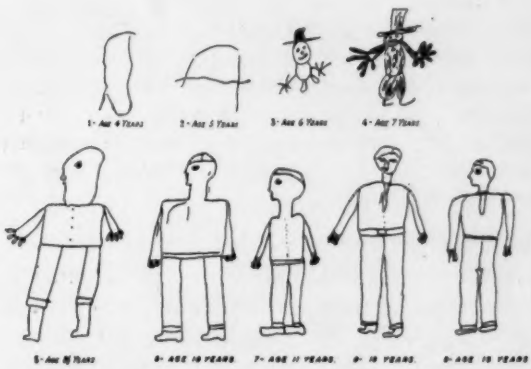

Fig. 8.—Spontaneous drawings of a man, made at advancing ages, showing normal course of mental growth.

ing grandfather and grandmother. However, J. B. played in a natural way with children of her age. Her mother's succinct estimate was to the point: "She is like other kids, but slow and lazy."

At 7 years J. B. showed ordinary interest in dolls and dishes and was in no way demonstrative toward parents, siblings or playmates. Nor was she withdrawn; she showed normal friendliness in her social behavior.

DEVELOPMENTAL FACTORS

(a) *Endocrine Pathology.*—It is important to note at the onset that the secondary signs of sexual development occurred in a usual and normal order, as follows: (1) enlargement of breasts, (2) appearance of pubic hair, (3) menarche and (4) appearance of axillary hair. The records do not indicate the exact time of appearance of axillary hair, but it was after 5 years and 11 months and earlier than 8 years and 3 months. The initial slight irregularity of the menses, the later regularity and the still later irregularity were comparable to what is found in the normal young woman. The sequence and correlation of the secondary sexual signs, the normal size of the sella turcica and the absence of any marked mental or physical abnormalities up to the time of the patient's last illness suggest that the developmental deviations were due mainly to premature functioning of the ovaries.

Whether the pineal or adrenal gland, the ovary, the hypothalamus or even the thyroid was etiologically responsible cannot be determined. The hypothalmic centers were probably involved in accordance with the hypothesis of Le Marquand and Russell.[13] Citing Berlinger, these authors stated:

> We know that nerve fibers pass from the hypothalamus to the pars nervosa and pars intermedia, and that in all probability the hypothalamus and the posterior pituitary form a functional unit, so that a pineal influence upon the posterior pituitary would not be impossible. But more than that, the hypothalamus is closely related to the sympathetic system as shown by the researches of Cannon and others, and sympathetic fibers from the carotid plexus can be traced to the anterior pituitary lobe (Dandy). Thus the whole of the pituitary gland is connected by nervous influence to the hypothalamus, and it seems reasonable to suppose that the stimulus of a pineal tumor, or of a midbrain tumor, presses the trigger to fire the pituitary mechanism of puberty.

On such grounds one may ascribe an important role to the cerebellar tumor in the present instance. This type of tumor is rarely found in association with pineal neoplasm. It is not necessary to postulate an adrenal tumor, even though the hypertrichosis and the male distribution of hair are suggestive of an adrenal dysfunction. There was no clinical evidence of a tumor of the ovaries. On the other hand, many of the characteristics of the fibrillar astrocytoma were in harmony with the course of the symptoms. The intracranial pressure symptoms were doubtless due to the accumulation in the cyst rather than to the mural nodule itself.

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13. Le Marquand, H. S., and Russell, D. S.: A Case of Pubertax Praecox (Macrogenitosomia Praecox) in a Boy, Associated with a Tumor in the Floor of the Third Ventricle, Roy. Berkshire Hosp. Rep., 1934-1935, pp. 31-61.

(b) *Physical Growth.*—When one compares J. B.'s increase in height and weight with the optimum norms given by Engelbach [14] one finds that: (1) At 3 years and 11 months she was unusually tall for her age, but her height was within the limits for normal children of that age; at 10 years, however, she was near the 10 year norm; at 15 years she dropped even below the normal minimum. (2) With respect to weight, at 3 years and 11 months she was above the normal maximum for that age, and between 12 and 13 years she had lagged back to normal and was thereafter below normal for her age, but not below normal for her height. (3) Both the breadth and the length of the head were in almost exact accord with the norms from the age of 4 to 17 years, the total period studied.

Inspection of the chart of physical growth (fig. 2) shows that the early acceleration in growth was followed by an early cessation of growth in height and general skeletal dimensions. There was no appreciable change in skeletal size after the age of 11 years. There were an increase in weight and a slight increase in circumference of the chest, but these changes reflected an increase in fat and other tissues rather than in skeletal size. Thus, skeletal growth ceased three and one-half years earlier than usual. It is also of interest to note that while both parents were short (about 155 cm.), J. B.'s height at maturity was 15 cm. shorter than theirs; however, her brother was a head taller than the parents. Her small stature at puberty was probably not due to familial hereditary factors. More likely the early acceleration of growth caused a premature union of the epiphyses. "Particularly characteristic of hypergenitalism," Engelbach said, "is the advanced osseous development as manifested in a union of the long bone epiphyses some eight to ten years before the normal age for ossification."

It should be noted, furthermore, that the growth in height from 8 years and 6 months to 11 years was due principally to growth in length of the trunk, or body. This fact is brought out by a comparison of the height of the vertex with that of the suprasternal notch and that of the symphysion. Such a pattern of growth is normal for girls in their teens, but abnormal prior to that age.[15] One must remember, however, that with respect to maturity of skeletal growth J. B. at the age of 8 years and 6 months was comparable to a girl in her teens.

As one would expect, however, there was no adolescent spurt of growth at the usual age. Whether or not such a spurt occurred in a normal relation in time to the child's first menstruation is not known.

14. Engelbach, W.: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932, vol. 1, pp. 261-312.

15. Shuttleworth, F. K.: Sexual Maturation and the Physical Growth of Girls Six to Nineteen, Monographs of the Society for Research in Child Development, Washington, D. C., National Research Council, 1937, p. 95.

Certainly at some time before 4 years growth was unusually rapid, but in just what form this acceleration occurred cannot be learned.

Strength of grip as measured by the Smedley dynamometer was markedly developed at the time of the first menses; the strength of pressure then, at 3 years and 11 months, was equal to that of the normal girl of 7 years. With the decrease in rate of skeletal growth there was a decreased increment in the strength of grip, and when skeletal growth ceased strength of grip declined. When irregularity of the menses occurred, strength of grip again began to increase, but at a lower level than normal for the child's age. The drop in the curve at 16 years probably represented a true fluctuation.

(c) *Pelvic Characteristics.*—The unusually early arrest of skeletal growth in this case offers interesting speculation as to its influence on the formation of the pelvis. Clearly the patient presented the typical dolichopellic type of inlet, with pronounced development of the posterior part of the pelvis throughout. This development is that seen in adult female pelves and is associated with early and successful childbirth. It represents, therefore, a distinct "female" influence as contrasted with the male. In view of the incidence of the dolichopellic type of inlet among adolescent girls (64.6 per cent), the early arrest of skeletal growth may have "set" this part of the pelvis prematurely. In addition, the posterior part of the pelvis was typically female, even exaggerated in this aspect, and exceptional hormonal influence seems to be the most obvious explanation.

(d) *Menstrual History.*—One feature of the menstrual history which calls for consideration is the irregularity which was first reported at 13 years and which continued and increased in the subsequent years. Was this irregularity due to an intercurrent complication in some way connected with the cerebellar tumor? Or was it due to precocious displacement of the menopause?

If the latter alternative is accepted, the irregularity is not ascribed to a specific dysfunction. The fact that the sequence and correlation of the secondary sexual signs were in general normal suggests that the ovarian regulation may have been operating in a relatively normal manner as far as the menses themselves were concerned, with no marked disturbance of the time factors. The patient had matured sexually in four years, as opposed to the normal period of about twelve years. She might then be expected to cease menstruation at a much earlier age.

As already suggested in the section on menstrual history, the marked reduction in the estrogenic and androgenic substances found in the assay of J. B.'s urine at the age of 18 years may be interpreted as

a menopausal symptom. This interpretation is further justified by the evidences of irregularity in the menstrual intervals.

(e) *Study of the Central Nervous System.*—The psychologic career of the patient was in striking contrast to her bodily development. Physically she presented an astounding precocity, amounting to a whole decade. The developmental disturbance was so profound that it must have altered even prenatal phases of her life cycle. In early childhood she already had the configuration and the gonadal physiologic structure of an almost mature woman; yet her mental development was scarcely altered in its outward patterns. The central nervous system showed an amazing degree of invulnerability.

Such invulnerability is characteristic of insurance factors which safeguard the normal course of development. Experiment has shown that neural tissue is especially resistant to prolonged starvation and other forms of adversity. In the competition between organ systems the central nervous system is favored by certain immunities and priorities. Therefore, the brain suffered little disturbance, even in the presence of precocious pubescence. Secondary sexual characters were chiefly affected by the precocity. Skeletal growth was affected, but, significantly, the outer skeleton of the brain, namely the skull, grew in accordance with normal expectations. This implies independent controls for the development of the cranium, or controls which remain subordinate to the growth of the cerebrum.

The present case of pubertas praecox affords no warrant for the view that the phenomenon of growth is a function of an all-pervading sex factor or libido. On the contrary, this case supplies new evidence for the specificity of individual components of growth. There are deeply entrenched mechanisms of maturation which tend to preserve the integrity of the nervous system and to forward an optimal realization of the life cycle.

## SUMMARY

A case of well defined uncomplicated pubertas praecox is described. The subject, a Jewish girl, showed physical signs of pubescence in the first year of life and menstruated at the age of 3 years and 7 months. She died at the age of 18 years and 7 months of an infection following removal of a cerebellar fibrillar astrocytoma.

Physical and mental measurements made over a period of fifteen years are summarized and interpreted, with special reference to their developmental significance.

Carpal roentgenograms showed marked precocity of skeletal growth. Growth in height practically ceased at the age of 11 years. After brief initial irregularity, menses were regular until the age of 13 years. The subsequent irregularity was suggestive of menopausal factors.

The pelvis was of a typical dolichopellic type and posteriorly exceptionally spacious, suggesting an early osseous set combined with selective endocrine molding influences.

Psychologic measurements made at sixteen consecutive intervals showed a rather remarkable approximation to a near average course of intellectual development. The emotional life and personality manifestations were only slightly atypical.

The stability of the mental development is interpreted as denoting a preferential immunity of the central nervous system to certain forms of endocrine imbalance. The developmental distortion of the precocious pubescence was most conspicuous in the skeletal system. Cranial development, however, followed an average course.

Growth is regulated by specific determiners. The evidence afforded by pubertas praecox indicates that there is no single pervasively controlling sex factor.

# Case Reports

## CHRONIC PROGRESSIVE DEGENERATIVE ENCEPHALOPATHY

### A Clinicopathologic Study of an Unusual Case of Schilder's Disease

N. W. WINKELMAN, M.D., AND MATTHEW T. MOORE, M.D., PHILADELPHIA

The multiplicity of terms applied to Schilder's disease (encephalitis periaxialis diffusa)[1] and similar clinicopathologic conditions is an indication of the nebulous state in which the problem of unifying the demyelinating diseases of the central nervous system remains. With each contribution to the literature there emerges a clearer concept of the possible etiologic factors. The apparent diversity of histopathologic appearance in reality may merely represent different phases of a fundamentally similar process.

The clinical manifestations of Schilder's disease are so multiform that Bouman[2] stated, in effect, that no uniform symptom complex could be formulated. Ferraro,[3] in his unique article in which he essayed the difficult task of classifying the primary demyelinating processes of the central nervous system, gave a review of the literature and a comprehensive outline of the clinical and pathologic observations in cases of Schilder's disease and related disorders.

Because of the varied mode of onset and the sometimes confusing clinical picture, particularly when the patient is an adult, an antemortem diagnosis is made only infrequently. The clinical diagnostic difficulties arise from the similarity of the disease to such conditions as acute multiple sclerosis, encephalomyelitis and tumor of the brain. Should there be a fortuitous coincidence, such as the appearance of a case of Schilder's disease during an epidemic of encephaltis or roentgenologic findings suggestive of an intracranial mass lesion, it can readily be seen that the correct diagnosis would be overlooked.

The following case is reported because of certain unusual clinical and histopathologic features which may add to the understanding of some of the problems presented by Schilder's disease.

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Read at the meeting of the American Association of Neuropathologists, Atlantic City, N. J., May 2, 1938.

From the John Leonard Eckel Laboratory of Neuropathology, the University of Pennsylvania Graduate School of Medicine.

1. Schilder, P.: Zur Kenntnis der sogenannten diffusen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1, 1912.

2. Bouman, L.: Diffuse Sclerosis: Encephalitis Periaxialis Diffusa, Baltimore, William Wood & Company, 1934.

3. Ferraro, A.: Primary Demyelinating Processes of the Central Nervous System: An Attempt at Unification and Classification, Arch. Neurol. & Psychiat. **37**:1100 (May) 1937.

REPORT OF CASE

*History.*—H. G., a white woman aged 37, was admitted to the hospital on Aug. 22, 1933, because of a sudden convulsive seizure lasting fifteen minutes. When admitted to the hospital she was stuporous; she remained so for five days. For one week prior to the onset she had had an infection of the upper part of the respiratory tract.

The family and the past medical history were without significance.

*Clinical Examination.*—The patient was a well nourished woman in deep stupor. The head was turned to the left. There was complete flaccid hemiplegia of the left side. Nuchal rigidity was present. A Brudzinski sign was present, and a Kernig sign was elicted bilaterally. Arcus senilis was present in each eye. There were a divergent squint and slow horizontal nystagmus. The tendon reflexes in the upper extremities were prompt and were greater on the right side than on the left. A Trömner sign was obtained on the right. The abdominal reflexes were absent. The tendon reflexes in the lower extremities were present. There was a questionable Babinski sign on the left. A lumbar puncture performed on the day of admission revealed a pressure of 4 mm. of mercury. On August 24 another lumbar puncture showed a pressure of 14 mm. The optic disks revealed papilledema of approximately 2 D. By August 26 the patient was able to utter a few words. The hemiplegia slowly disappeared, and at the time of her discharge from the hospital, on September 11, the patient had recovered her speech and her ability to walk.

The temperature ranged from 99.2 F. on the day of admission to 101 F. on August 27, after which it receded to normal on August 30, remaining normal thereafter. The blood pressure was 125 systolic and 70 diastolic.

*Laboratory Data.*—The following values were obtained:

Blood Counts

| | | | | | Differential Count | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Date | Hemoglobin, Gm. | Red Blood Cells | White Blood Cells | Color Index | Young Forms | Neutrophils | Eosinophils | Basophils | Monocytes | Lymphocytes |
| 8/23/33 | 11.5 | 4,320,000 | 18,400 | 0.8 | 25 | 61 | 0 | 0 | 3 | 11 |
| 8/26/33 | .... | ..... | 17,350 | ... | 16 | 66 | 0 | 0 | 5 | 13 |
| 8/29/33 | .... | ..... | 12,950 | ... | 15 | 73 | 1 | 0 | 2 | 9 |
| 9/ 6/33 | 12.5 | 4,170,000 | 9,900 | 0.9 | 0 | 64 | 2 | 0 | 6 | 28 |

Spinal Fluid Studies

| Date | Sugar | Globulin | Chlorides | White Blood Cells |
|---|---|---|---|---|
| 8/22/33 | 100 mg. | Marked increase | 710 mg. | 623 (lymphocytes predominating) |
| 8/23/33 | ..... | ..... | ..... | 153 (polymorphonuclears predominating) |
| 8/24/33 | 100 mg. | Marked increase | 710 mg. | 51 (polymorphonuclears, 83 per cent; lymphocytes, 17 per cent) |
| 8/28/33 | ..... | ..... | ..... | 11 (all polymorphonuclears) |
| 8/24/33 | Wassermann reaction, negative; colloidal gold curve, 0000111000 | | | |

Urinalysis on August 23 and September 6 revealed nothing abnormal.

*Course.*—The patient remained free from complaints until November 1, when without premonitory signs her head slowly turned to the left and she had a jacksonian convulsion on the left side, during which she was unconscious for one-half hour. Three more such attacks occurred on the same day, after which she was readmitted to the hospital.

There appeared to be no disturbance in behavior or mental faculties. Acuity of smell was diminished on the left. A fine horizontal nystagmus to the left could easily be demonstrated. Nystagmus to the right was exhaustible. Gross finger tests of the visual fields showed definite homonymous quadrantanopia. The tendon reflexes were diminished on the left side of the body and were somewhat exaggerated on the right. The Trömner sign was present on the right, and there was flabbiness of the musculature of the right arm and forearm.

During the second period of hospitalization, from November 1 to November 29, the patient had six jacksonian convulsive seizures, each beginning with turning of the head and eyes to the left. This was followed successively by twitching and clonic contractions of the left side of the face, clonic contractions of the left hand and fingers and involvement of the left arm and shoulder, and occasionally the left lower extremity, after which the attack became generalized. When the face alone was involved she retained consciousness throughout the attack, but when the convulsive seizures were generalized unconsciousness ensued. Repeated

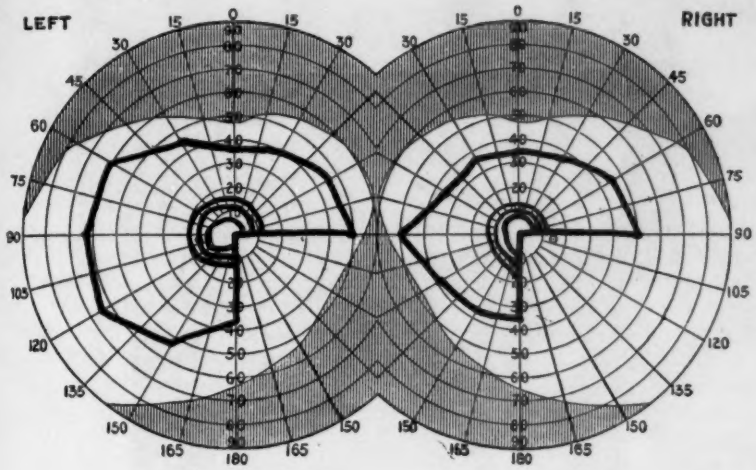


Fig. 1.—Right homonymous lower quadrantanopsia.

studies of the spinal fluid gave normal results. The Bárány test revealed the presence of an "intracranial supratentorial lesion." The ocular fundi were normal. Right homonymous lower quadrantanopia was present (fig. 1). Roentgenologic studies of the skull showed definite displacement of the pineal gland posteriorly and toward the right side (fig. 2). This displacement was interpreted as due to a mass lesion in the left parietal region of the brain. The patient was discharged on November 29 with the tentative diagnosis of a lesion of the left parietal lobe, but operation was deferred because of the confused clinical picture.

The patient was again admitted to the hospital on Jan. 12, 1934. In the interval she had had one jacksonian convulsive seizure involving the left side of the body. Neurologic examination showed augmentation of the previous findings by anisocoria, the right pupil being larger than the left, definite weakness of the lower half of the left side of the face, deviation of the tongue to the left and atrophic change in the muscles of the right hand, forearm and shoulder and, to a moderate degree, the right calf. Flat roentgenograms taken on January 15 revealed the findings

previously described. Encephalographic examination was performed on January 19, and the conclusions from the findings follow. "Some of the encephalographic evidence is against a diagnosis of a mass lesion. There is still a possibility that there is such a lesion on the left side, the most likely location being the left occipital lobe, just above the tentorium and toward the lateral aspect of this lobe" (fig. 3).

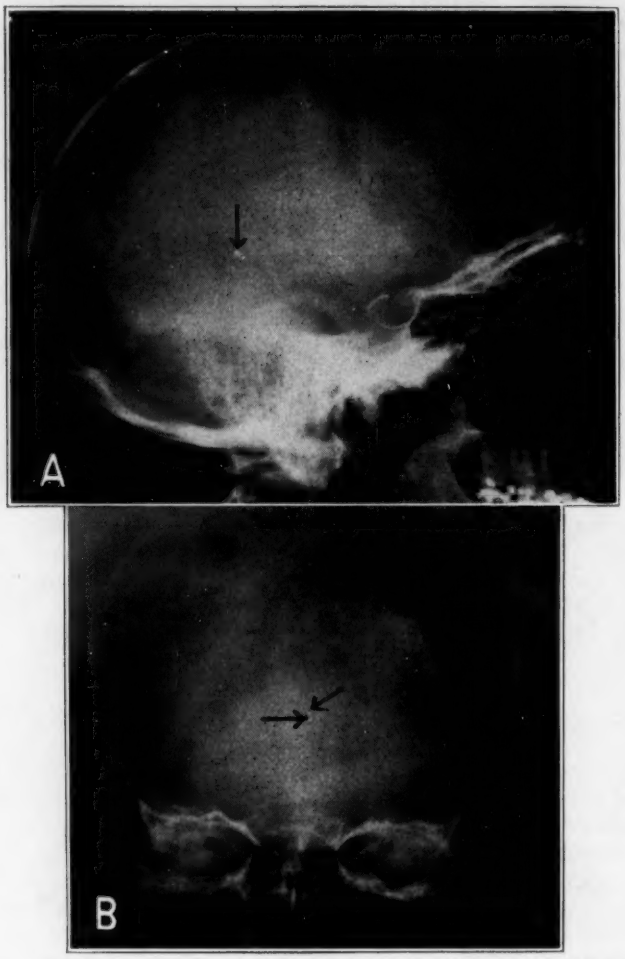


Fig. 2.—*A*, lateral view of the skull, showing the posteriorly displaced pineal gland. *B*, posteroanterior view of the skull, showing the pineal gland displaced to the right of the midline.

*Operation.*—On the basis of the roentgenographic studies and the presence of atrophy of the parietal lobe with involvement of the right limbs, it was thought that a mass lesion of the left parietal lobe was present and that operative intervention was indicated. Accordingly, an exploratory craniotomy was performed.

in which a left temporoparieto-occipital flap was turned. There was no gross evidence of tumor. The patient was discharged on February 8.

*Postoperative Course.*—Despite medication, the patient had occasional severe convulsive seizures, always beginning in the left side of the face and then involving the left side of the body, finally becoming generalized. On her fifth admission to the hospital, on April 14, 1934, there was no increase in the field defect. A study of the eyegrounds showed attenuation of the retinal arteries. There was weakness of the left side of the face of a distinct central type. The tendon reflexes in the upper extremities were exaggerated, and a Trömner sign was present bilaterally. The other neurologic findings remained essentially the same. Basal metabolic studies performed on several occasions showed readings of —33, —35 and —22 per cent. Thyroid therapy proved unavailing. The amyl nitrite (Hare) test for cerebrospinal fluid pressure gave a reading of 365 mm. of water. Roentgenologic study of the skull on April 17 showed that the pineal gland had not altered its position since the craniotomy. Other laboratory studies gave essentially normal results. High voltage roentgen therapy was given. There was almost complete epilation. After the last course of roentgen treatment the patient was free from attacks for ten days, only to have them recur with greater severity. Medication in heavy doses was ineffective.

In February 1935 the patient began to show periods of depression. She became apathetic, and cerebration appeared to be delayed. Memory for recent events was perceptibly disturbed, and orientation for time and place was impaired. Before the convulsive fits she became apprehensive and bewildered. Immediately prior to a seizure she uttered a piercing scream. She was admitted to the hospital for the seventh time on February 21. Neurologic examination revealed essentially the same findings as on the previous admissions, together with early atrophic changes of the optic disks. The patient was generally emaciated and weak. The systolic blood pressure throughout remained between 90 and 125 mm. Spinal tap showed a pressure of 10 mm. of mercury.

The patient and her family were anxious to have some further operative procedure carried out. However, the bilaterality of the signs and symptoms and the absence of evidence of increased intracranial pressure militated against another exploration. She was therefore discharged on March 8.

Convulsive seizures continued to occur despite the daily consumption of as much as 18 grains (1.16 Gm.) of sodium amytal and 6 grains (0.39 Gm.) of phenobarbital in combination. There was a slow decline mentally, and vision became greatly diminished. On Sept. 8, 1935, status epilepticus occurred and persisted for eight hours, ending in death.

*Postmortem Examination.*—Macroscopic Observations: The outstanding features of the external appearance of the brain were severe universal congestion and hemorrhages in the subarachnoid space. In both the left parietal and the left premotor area there were elevated circular whitish scars, the result of puncture of the surgeon's trocar. The brain was free from convolutional atrophy and seemed to have been under pressure. The membranes were clear and devoid of opacities.

At the base of the brain the blood vessels were small and showed no sclerotic changes. The interpeduncular space was covered by a rather dense pia-arachnoid membrane. The temporal lobes were bound down with a little greater firmness than is normal.

On section of the cerebellum, medulla and pons no abnormalities were uncovered except slight enlargement of the iter.

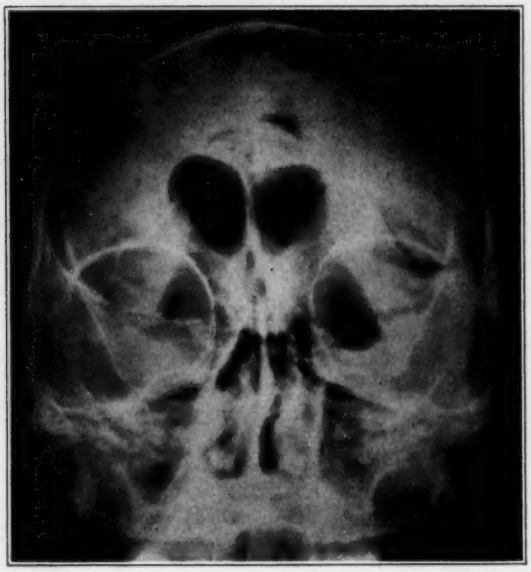

Fig. 3.—Encephalogram (anteroposterior view). The left lateral ventricle is flattened, the midline structures are dislocated to the right.

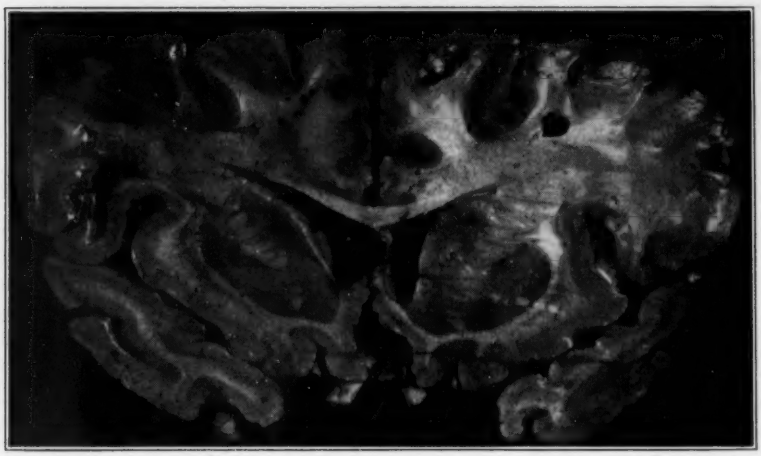

Fig. 4.—Coronal section of the freshly cut brain, showing degeneration in the right hemisphere, sharply limited to the subcortex.

Coronal section of the frontal lobes revealed internal hydrocephalus of moderate severity. There was marked thinning of the corpus callosum. As coronal sections were made from the anterior to the posterior portion of the brain, a definite subcortical softening was noted in the arm area on the right side (fig. 4). This softening spared completely the cortical gray matter, followed the outline of the

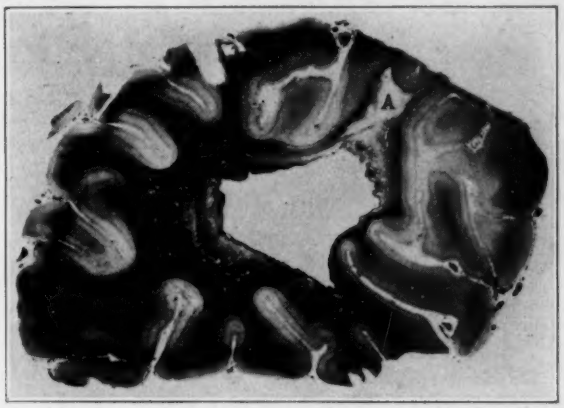


Fig. 5.—Section of the left occipital lobe (Weil stain), indicating the area of intense degeneration (*A*) in the subcortex of the visual area and less intense diffuse demyelination in the periventricular region.

Fig. 6.—Enlargement of area *A* shown in figure 5. Note the sparing of the arcuate fibers in the region of severe demyelination of the white matter and the absence of involvement of the cortex. Weil stain.

convolutions and included a considerable part of the length of the motor area. Another area of the same sort was observed in the left occipital lobe, involving the upper part of the visual area. This area of softening was exactly similar to that

seen in the motor area. The basal ganglia and the substantia nigra were normal. The pineal body was very small, was calcified and appeared to be directly in the midline.

Microscopic Examination: Study with the naked eye of the myelin sheath sections (Weil stain) from all parts of the cerebrum showed a varying degree of demyelination, limited sharply to the subcortex but sparing the arcuate fibers. The greatest amount of demyelination occurred in the left occipital lobe. Here,

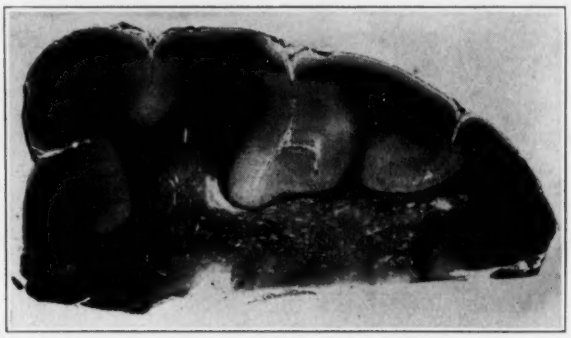

Fig. 7.—Myelin sheath preparation (Weil stain) of the right motor area, showing diffuse moderate subcortical demyelination with superimposed spotty areas of intense degeneration.

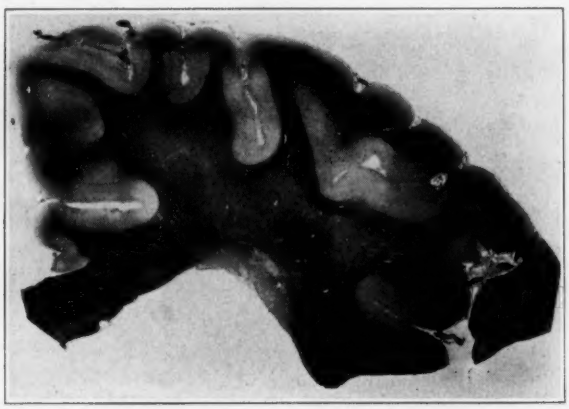

Fig. 8.—Demyelination of the subcortex in the left parietal lobe. This is not as intense as in the left occipital or the right motor area. Weil stain.

too, the amount of demyelination was variable, as can be seen in figure 5. Almost complete demyelination was observed at one point (*A*), but even here there was integrity of the arcuate, or U, fibers. The frontal lobes showed a more diffuse but less intense form of demyelination, the right motor area (fig. 7) being more involved than the left. The left parietal lobe (fig. 8) showed rather uniform demyelination, of moderate degree. The rest of the brain presented a varying

amount of loss of myelin in the subcortex, the extent of demyelination changing from area to area and displaying variations even in the same region. The areas of demyelination had a moth-eaten appearance in places, but for the most part there was diffuse lightness of stain, in contrast to the focal loss seen in cases of vascular disease.

Preparations stained by Nissl's method revealed the criteria for Schilder's disease, especially in the left occipital lobe and the right motor area. These were rather sharp demarcation and limitation of the process to the white substance of the brain, with widespread accumulations of glial elements, including spider cells, fibroblastic astrocytes, gitter cells and adventitial infiltrations of gitter cells and

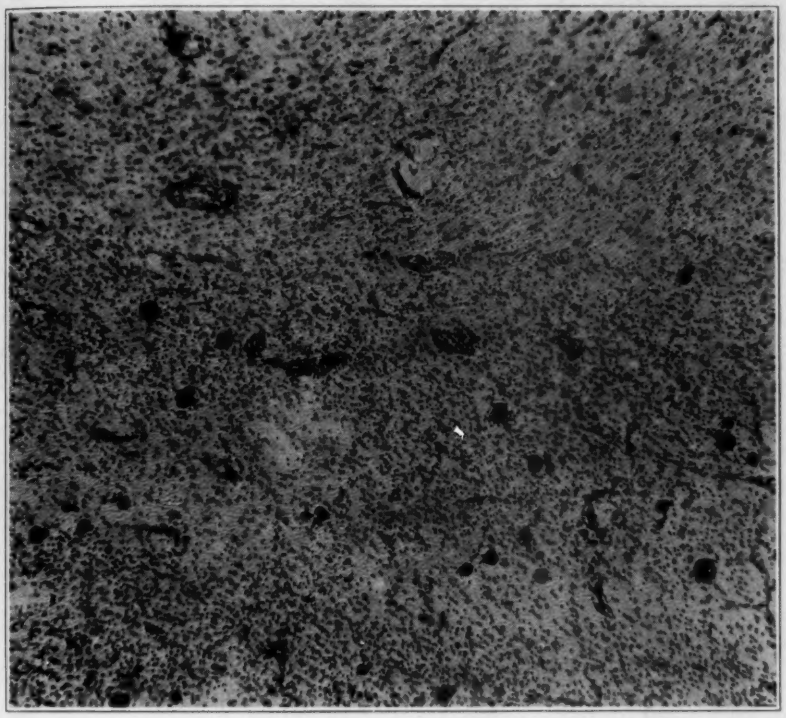

Fig. 9.—Subcortex of the visual area of the left occipital lobe. Note the intense glial reaction, the perivascular cuffing and the presence of many mucin bodies. Toluidine blue stain; × 45.

lymphocytes (figs. 9 and 10). Within the occipital lobe in particular there was a great increase of glial elements, notably astrocytes. Numerous gitter cells were observed in the subcortex, and the perivascular spaces contained round cell elements consisting both of phagocytes and, to a lesser degree, of lymphocytes. Gemästete glia cells (fig. 11), less numerous than the gitter cells, were seen mainly in the occipital lobe, in relation to the area showing the maximum degeneration. Status spongiosus occurred rather uniformly throughout the subcortex, with the appearance of numerous fibrillary astrocytes and compound granular cells. In some areas there

was complete destruction of both axis-cylinders and myelin sheaths. In the less involved areas, such as the frontal lobe, numerous naked axis-cylinders were present, many of which could still be considered normal. In the frontal lobes and the less involved areas generally there were few phagocytes and few blood vessels showing perivascular cuffing. Here the oligodendroglia cells were increased in number, and the astrocytes were in the minority, in contrast to the occipital lobe. Mucin bodies appeared in abundance in the white matter.

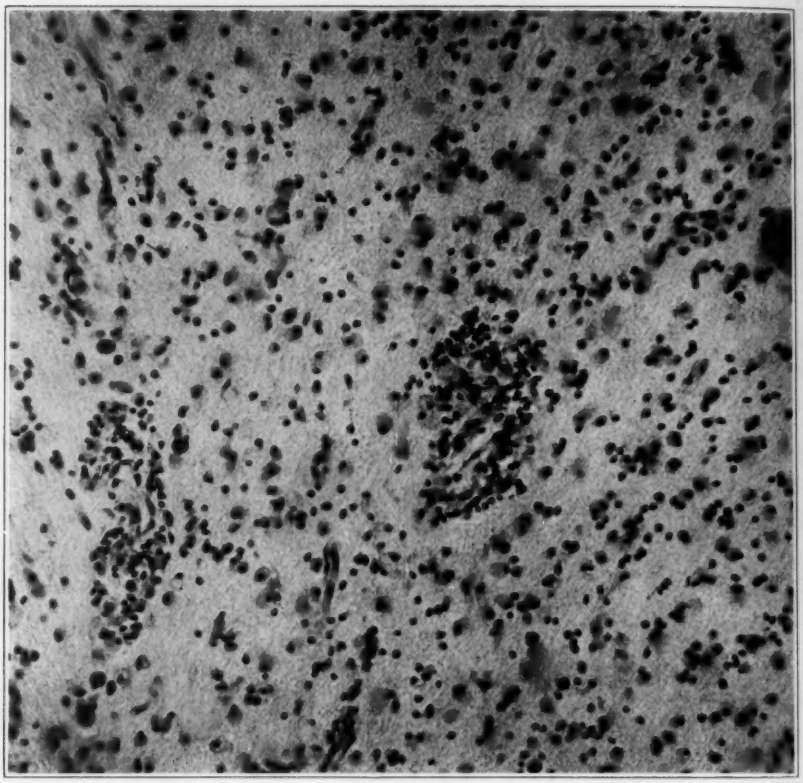

Fig. 10.—Cell stain of the white matter, showing the character of the cells in the areas of degeneration. Gitter cells are distributed throughout the tissue and are seen grouped about the vessels. Gemästete cells and oligoglia cells undergoing mucinoid degeneration are also present in considerable numbers. Toluidine blue stain; × 200.

The smaller blood vessels throughout the entire subcortex showed mild swelling of the lining cells. The larger blood vessels were within normal limits, only an occasional vessel showing slight thickening and hyalinization.

The entire process stopped sharply at the corticosubcortical margin; the gray matter of the cortex was not involved. The ganglion cells were normal in appearance and number. The blood vessels, except for congestion, showed nothing

unusual. The membranes showed mild thickening and fibrosis. Some débris was present within the subarachnoid space and had provoked marginal gliosis in places. In one or two areas, particularly in relation to the operative site, adhesions of the meninges to the cortex were present. The blood vessels within the membranes showed a little greater tendency to thickening and hyalinization of the walls than was observed within the substance of the brain. At no point, however, were these changes severe or out of keeping with the age of the patient.

The remainder of the central nervous system showed no deviations from the normal.

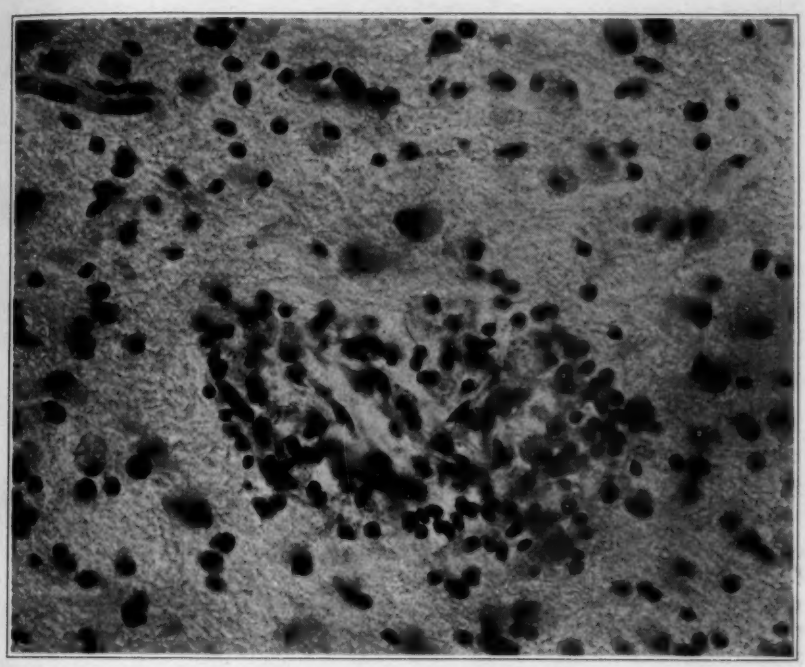

Fig. 11.—Perivascular cuffing with gitter cells, glia nuclei and occasional lymphocytes. Gemästete glia cells, swollen oligodendroglia cells, mucinoid degeneration of oligodendrocytes and scavenger cells are seen in the area surrounding the cuffed vessel. Toluidine blue stain; × 400.

## COMMENT

*Clinical Aspects.*—Both the clinical and the pathologic phases of Schilder's disease have been described in the literature, as in the articles by Ferraro,[3] Bouman,[2] Steiner,[4] Jacob,[5] Globus and Strauss [6] and many

4. Steiner, G., in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 2, pt. 7, p. 305

5. Jacob, A.: Anatomie und Histologie des Grosshirns, Vienna, Franz Deuticke, 1929, vol. 2, p. 849.

6. Globus, J. H., and Strauss, I.: Progressive Degenerative Subcortical Encephalopathy (Schilder's Disease), Arch. Neurol. & Psychiat. **20**:1190 (Dec.) 1928.

others. We shall, therefore, confine our discussion to some of the unusual and infrequently observed aspects of this case.

Convulsive seizures occur less frequently in adults than in children as a manifestation of diffuse sclerosis, and as an initial symptom they are rare. The first sign of illness in our patient was the epileptic fit, which was followed by prolonged stupor. Davison and Schick [7] described as the first sign of illness in a 15 year old girl, a convulsive seizure lasting thirty minutes, followed by stupor. During the course of Schilder's disease convulsive seizures may occur at regular or infrequent intervals and may be either of jacksonian or of generalized type. The seizures in our patient began invariably as a focal jacksonian attack involving the left side of the face and the left arm, frequently without loss of consciousness; the convulsion occasionally became generalized, at which time consciousness was lost.

The history of infection of the upper respiratory tract for one week before the onset of convulsive symptoms, together with the subsequent clinical and laboratory findings, which suggests the presence of meningoencephalitis of unknown origin, may be of interest as regards the cause of Schilder's disease. Our patient showed stupor for five days; there were positive meningeal signs, choked disks, 623 cells per cubic millimeter of cerebrospinal fluid and a marked increase of globulin in the fluid. Schaltenbrand [8] expressed the opinion that Schilder's disease occurs in a congenitally predisposed brain which has been invaded by an ultramicroscopic virus. Globus and Strauss [6] stated:

> It seems probable that the abrupt development of symptoms indicates some sudden change in the normal metabolism in the central nervous system as though some toxic agent or endogenous poison had led to the arrest in normal differentiation and dissolution of the brain tissue.

They stressed the presence of gastrointestinal disturbances preceding the onset of the disease. Other investigators [9] have reported the tendency of gastrointestinal disturbances to usher in the neurologic manifestations. The suggestion by Meyer and Tennent [9a] of the possible role of avitaminosis as a causative factor must be strongly considered. Acute infectious diseases, tuberculosis, atrophy of the adrenal glands, birth trauma and carbon monoxide poisoning have all been mentioned by Meyer and Pilkington [10] as deserving consideration in the

7. Davison, C., and Schick, W.: Encephalopathia Periaxialis Diffusa (Schilder's Disease), Arch. Neurol. & Psychiat. **25**:1063 (May) 1931.

8. Schaltenbrand, G.: Encephalitis Periaxialis Diffusa (Schilder): Case Report with Clinical and Anatomical Studies, Arch. Neurol. & Psychiat. **18**:944 (Dec.) 1927.

9. (*a*) Meyer, A., and Tennent, T.: Familial Schilder's Disease, Brain **59**: 100, 1936. (*b*) Globus, J. H., in Penfield, W.: Cytology and Cellular Pathology of the Central Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, p. 1145. (*c*) Bielschowsky, F.: Die Bedeutung des Infektes für die diffuse Sklerose, zugleich ein Beitrag zur Klinik und Pathologie der diffusen Sklerose, J. f. Psychol. u. Neurol. **33**:12, 1927.

10. Meyer, A., and Pilkington, F.: Some Problems of Pathogenesis in Schilder's Disease, with a Description of a New Familial Case, J. Ment. Sc. **82**: 812, 1936.

proper evaluation of predisposing or precipitating causes of diffuse sclerosis and related conditions. The apparent diversity of etiologic factors might lead one to suppose that they have no direct bearing on the pathogenesis of Schilder's disease; however, a common denominator may yet be found. The similarity of the onset and symptoms in our case to those observed in cases of encephalomyelitis and acute multiple sclerosis is of interest in the light of Ferraro's contention that a similarity exists among the demyelinating diseases.

Not infrequently the course of diffuse sclerosis, particularly if the patient is an adult, may be indistinguishable from that of tumor of the brain. Especially is this so when signs such as hemiplegia, jacksonian convulsive seizures, unilateral sensory disturbances and hemianopia suggest by their unilaterality a lesion of one hemisphere. When the signs are indicative of numerous bilateral leisons no such difficulty in diagnosis arises.

Urechia [11] reported the case of a patient aged 40 who had headaches followed by the clinical signs of a progressively developing tumor of the right hemisphere. An antemortem diagnosis of such a tumor was made. Roentgenologic examination revealed nothing abnormal. Postmortem examination showed what appeared to be a spongy tumor in the right motor and frontal areas. Histopathologic examination of the brain showed the condition to be Schilder's disease. In cases reported in the literature in which tumor was suspected there were no confirmatory or questionable roentgenographic findings, as in our case.

Vastine and Kinney [12] and Dyke [13] have elaborated a method of measuring the position of the calcified pineal gland and have established displacement of the pineal shadow as a criterion for the presence of an intracranial neoplasm. With regard to nontumorous skulls. Dyke [13] stated that "a figure somewhat below 14 per cent represents the number of pineals which are situated outside of the normal zone in normal skulls and most of these apparently are situated anterior to this zone."

Roentgenographic examination in our case, repeated several times, showed consistent deviation of the pineal gland posteriorly and to the right. This was highly suggestive of a lesion in the left hemisphere, probably in the parietal lobe. The encephalographic findings, though not conclusive, showed dislocation of the ventricles to the right, which was also suggestive of a space-taking lesion in the left hemisphere.

The atrophy in our case was evident and was not an incidental observation. The muscular atrophy which has been reported in several cases of Schilder's disease [2] has not been adequately explained heretofore. Silverstein and one of us (N. W. W.)[14] described trophic muscular wasting associated with retrorolandic lesions and attached considerable

11. Urechia, M. C. L.: Encéphalite périaxiale de Schilder, évoluant sous l'aspect d'une tumeur, Rev. neurol. **64**:968, 1935.

12. Vastine, J. H., and Kinney, K. K.: The Pineal Shadow as an Aid in the Localization of Brain Tumors, Am. J. Roentgenol. **17**:320, 1927.

13. Dyke, C.: Indirect Signs of Brain Tumor as Noted in Routine Roentgen Examinations: Displacement of Pineal Shadow; Survey of Three Thousand Consecutive Skull Examinations, Am. J. Roentgenol. **23**:598, 1930.

14. Winkelman, N. W., and Silverstein, A.: Trophic Disturbances of the Limbs in Retro-Rolandic Lesions, A. Research Nerv. & Ment. Dis., Proc. **13**:485, 1932.

localizing significance to its presence. One of the prominent features in the present case was the wasting of the muscles of the right arm, the shoulder girdle and the right calf. This finding, in association with displacement of the pineal gland, the encephalographic interpretation and the right homonymous inferior quadrantanopia, determined the diagnosis of a tumor in the left parieto-occipital area. Histopathologic examination of the left parietal lobe revealed rather diffuse but moderate involvement of the white matter. There were loss of myelin and increase of glia, but no great degree of degeneration. Scavenger cells were observed in the perivascular spaces, but not in such large masses as were observed in the left occipital lobe. Löwenberg and Fulstow [15] reported a case of atypical diffuse sclerosis in which there was atrophy of the intrinsic muscles of the right hand and right shoulder girdle and, to a lesser degree, of the left hand. Microscopic examination showed the pathologic changes to be most severe in the parietal and frontal lobes where severe destructive changes involving the myelin and axis-cylinders occurred. Secondary degenerative changes in the cord, consisting of shrinkage of the large ganglion cells and involvement of the pyramidal tracts, were also described. Cellular changes were noted throughout the gray matter of the entire cord. No explanation was given for the muscular atrophy localized mainly in the right upper limb.

The optic atrophy, which came on gradually and was definite before the patient's death, is an infrequent finding in Schilder's disease. Some cases have been described; Davison and Schick [7] enumerated several from the literature and reported the presence of this condition in their case.

*Histopathologic Aspects.*—The widespread destruction of myelin, which is considered the outstanding pathologic change in Schilder's disease, usually is symmetric and may involve any portion of the white matter of the brain. Demyelination may, however, occur in irregularly distributed patches, representing transitional or not fully developed forms of diffuse sclerosis, on the basis of which Hallervorden and Spatz [16] contended that the demyelinating diseases are definitely related. The demyelination occurring in our case was most intense in the subcortex of the visual area of the left occipital lobe and in the face and arm regions of the right motor area. The rest of the subcortex showed moderate diffuse involvement. There was no involvement of the cortex at any point, although the cortex has been reported by Jacob [5] to be the site of extensive degeneration. The arcuate fibers were intact even in the intensely degenerated areas. The cell picture in the severely degenerated areas was typically that associated with Schilder's disease, with abundance of gitter cells in the foci of demyelination, surrounded by areas of glial reaction made up of gemästete glia cells, fibrillary astrocytes and glia fibers. The vessels in the vicinity of the degeneration were cuffed with scavenger cells, glia nuclei and (to a lesser degree)

15. Löwenberg, K., and Fulstow, M.: Atypical Diffuse Sclerosis, Arch. Neurol. & Psychiat. **27**:389 (Feb.) 1932.

16. Hallervorden, I., and Spatz, H.: Ueber die konzentrische Sklerose und die physikalische-chemischen Faktoren bei der Ausbreitung von Entmarkungsprozessen, Arch. f. Psychiat. **98**:641, 1933.

lymphocytes. Mucin bodies in large numbers and status spongiosus, which were present in our case, have frequently been described and are not unusual.

## SUMMARY

A case illustrating the histopathologic features of Schilder's disease is presented. The acute onset with the concomitant clinical and laboratory data, consisting of stupor, hemiplegia, signs of meningeal irritation, choked disks, pleocytosis and increase of protein in the cerebrospinal fluid and indicating what appeared to be meningoencephalitis of virus origin, is of interest because of the undetermined cause of Schilder's disease. Coincidental findings of trophic muscular atrophy on the right, right homonymous inferior quadrantanopia, deviation of the pineal gland posteriorly and to the right as shown by roentgen studies and deviation of the ventricular system to the right as revealed by encephalograms led to the erroneous diagnosis of a tumor of the left hemisphere. Focal jacksonian convulsive seizures involving the left side of the face and the left arm, with mental signs, gave evidence that numerous bilateral lesions existed. Optic atrophy was obviously present in the latter part of the illness, and the final comparatively rapid progress of the disease, culminating in death, completed a picture which in its entirety was compatible with that seen in Schilder's disease.

Histopathologically the tissues revealed involvement of the subcortex alone, with sparing of the cortex, the basal ganglia, the cerebellum and the brain stem in asymmetric areas but in accord with the histopathologic criteria established by Schilder and others.

In view of the numerous designations given to the many variants of Schilder's disease, we shall endeavor to avoid controversy by applying the term which most adequately describes the condition in this case, i. e., progressive degenerative subcortical encephalopathy (Globus and Strauss [6]).

# FACIAL PARALYSIS IN CEPHALIC TETANUS

ARTHUR L. WATKINS, M.D., BOSTON

Knowledge of the unusual form of tetanus known as cephalic tetanus and of the mechanism of the facial paralysis associated with this disease is still so imperfect that the report of an isolated case seems warranted in an attempt to ascertain the cause of the condition.

The literature on tetanus is profuse. It has been reviewed recently by Abel and his associates.[1] The first description of the cephalic form of the disease is usually ascribed to Rose [2] (in 1869), and the condition has been reported in the literature not infrequently during the past forty years, although the total number of cases is not great. Brown [3] in 1912 found 94 cases recorded up to that time, and a moderate number have been reported since. In spite of these clinical studies no definite conclusion has been reached as to the mechanism of the facial paralysis. The syndrome is rare in this clinic, and even the existence of facial paralysis is doubted by the author of a recent textbook of neurology.[4]

Cephalic tetanus follows infection of wounds of the face by the tetanus bacillus and is characterized by spasm or paralysis of the muscles of the face, jaws and pharynx. Paralysis of the extra-ocular muscles occurs in an occasional case. If the disease is severe, tetanus descendens follows these local manifestations. The mechanism of the facial paralysis has been a subject of debate in the literature.[5] It is now generally believed that if true paralysis does occur it is the result of an overwhelming amount of toxin paralyzing the central motor nucleus or the motor end plates. The main point of discussion in this report is the occurrence of flaccid paralysis in association with a disease characterized by muscular rigidity and spasm.

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From the Surgical and Neurological Services, the Massachusetts General Hospital, and from the Department of Neurology, Harvard Medical School.

1. Abel, J. J., and Hampil, B.: Researches on Tetanus: IV. Some Historical Notes on Tetanus and Commentaries Thereon, Bull. Johns Hopkins Hosp. **57**:343-372, 1935.

2. Rose, E., in von Pitha, F., and Billroth, C. A. T.: Handbuch der allgemeinen und speciellen Chirurgie, Stuttgart, Ferdinand Enke, 1869-1874.

3. Brown, A. J.: Cephalic Tetanus, Ann. Surg. **55**:473-484, 1912.

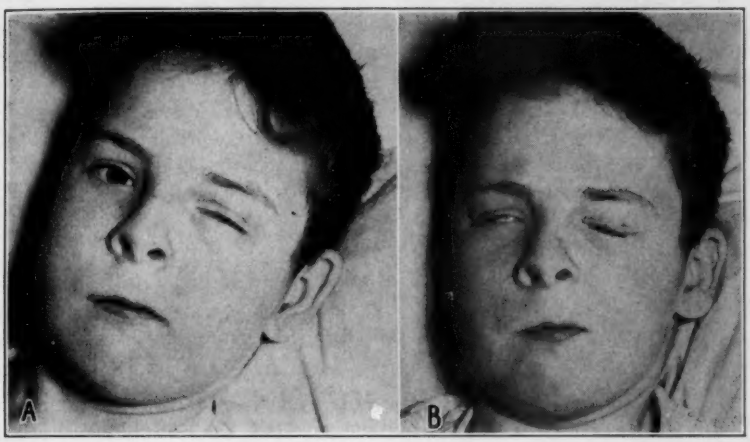
4. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Springfield, Ill., Charles C. Thomas, Publisher, 1937, p. 543.

5. (*a*) Bruner, C.: Experimentelle und klinische Studien über den Kopftetanus, Beitr. z. klin. Chir. **12**:523-588, 1894. (*b*) Gowers, W. R.: A Manual of Diseases of the Nervous System, Philadelphia, P. Blakiston's Son & Co., 1899, vol. 2, p. 683. (*c*) Ranson, S. W.: Local Tetanus: A Study of Muscle Tonus and Contracture, Arch. Neurol. & Psychiat. **20**:663-701 (Oct.) 1928. (*d*) Klar, J.: Kopftetanus nach perforierender Kornealverletzung, Klin. Monatsbl. f. Augenh. **79**:355-361, 1927. Rose.[2] Brown.[3] Ford.[4]

## REPORT OF A CASE

*History.*—In May 1938 an 11 year old boy was struck in the right nasolabial fold by a dirty stick thrown by a playmate. A laceration resulted, which was irrigated and closed with one suture. The following day the cheek was swollen, and two days later there was definite paralysis of facial movements on the same side. On the fifth day after the injury the boy was unable to open his jaws and was admitted to the Massachusetts General Hospital.

*Examination.*—On admission the patient appeared ill, with a flushed face, a rectal temperature of 100 F., a respiratory rate of 20 and a pulse rate of 100. There was a small granulating wound 1 cm. long in the right nasolabial fold, with surrounding cellulitis and edema. General physical examination gave negative results. Neurologic examination revealed bilateral trismus; the boy could not open his mouth more than a fraction of a centimeter and attempts to do so were often followed by increase of the trismus and involuntary grinding of the teeth.




*A*, photograph of the patient at rest, ten days after the onset of the illness. Note the facial spasm on the left and the flattening of the right side of the face. *B*, photograph taken on same day, while the patient was attempting to close the eyes and smile. Note the paralysis of the right side of the face and the increased facial spasms on the left.

There was continuous spasm of the left side of the face, which drew the corner of the mouth to one side and closed the eye. The spasm was accentuated if one tapped the face. The right side of the face (the side on which the lesion was present) showed flaccid paralysis of a peripheral type, which was more marked in the lower than in the upper portion, although there was inability to close the eye, and Bell's phenomenon was present. The pupils were equal and reacted to light and in accommodation. The extraocular movements were normal, and the other cranial nerves were intact. There was no difficulty in swallowing after fluids had been placed in the mouth. The neck was not stiff, and there was no evidence of generalized muscular rigidity or reflex spasm initially or at any subsequent examination.

*Laboratory Findings.*—Pus from the facial wound was cultured, and Staphylococcus albus was found. The white blood cell count on admission was 15,000 per cubic millimeter, and urinalysis gave negative results.

*Course.*—The patient was given 50,000 units of tetanus antitoxin (Massachusetts state serum) by hypodermoclysis in 500 cc. of physiologic solution of sodium chloride and 2.5 per cent dextrose solution on admission and 40,000 units daily in similar injections for three days, a total of 170,000 units being injected. The temperature ranged between 101 and 103 F. for eight days. Clinically there was some lessening of the trismus. No signs of tetanus descendens were noted. The facial paralysis remained unchanged during this period. On the eighth day of hospitalization there was a mild serum reaction, but otherwise there was steady improvement, with abatement of trismus and of spasm of the left side of the face. The boy was discharged on the eighteenth day after his admission to the hospital, with no residual trismus or facial spasm but with definite paresis of the left side of the face. It was nearly complete in the lower part of the face and was partial in the upper, although some improvement had occurred. The boy was followed in the outpatient department, where steady improvement in the facial paresis was noted. Forty-one days after the onset of the paralysis complete recovery had taken place and electrical reactions were normal.

*Special Tests.*—Electrical: Twelve days after admission and on numerous later occasions stimulation of the facial muscles and nerves with faradic and galvanic currents revealed diminished responses on the right and hyperactive ones on the left but no true degenerative reaction. Sensory: Two weeks after admission the patient was able to open the jaws sufficiently to protrude the tongue so that the sense of taste could be tested. There were definite loss of recognition of sugar on the anterior portion of the right half of the tongue and diminished perception of salt as compared with the left side. On subsequent tests (after discharge, when the facial paralysis had disappeared) taste was acute and equal bilaterally.

## COMMENT

The diagnosis of tetanus in this case was made from the history and clinical findings. The patient had lockjaw four or five days after infliction of a facial wound which became infected. Ipsilateral facial paralysis and contralateral facial spasm were present, corresponding with textbook descriptions of cephalic tetanus.[5b]

In order to explain these symptoms and signs the manner of transmission of the tetanus toxin to the nervous system must be known, as well as its effect on the susceptible tissues with which it comes in contact. Prior to publication of the work of Abel the commonly accepted theory of transmission of the toxin was that the toxin is carried by the endoneural or perineural lymphatics or by diffusion through the axis-cylinders to the central nervous system, where it exerts its action and the rigidity and reflex spasms of tetanus become manifest. Abel and others [6] have shown, however, that the toxin cannot reach the central nervous system via the nerve trunks or

6. (*a*) Abel, J. J.: Researches on Tetanus: I. On Poisons and Disease and Some Experiments with the Toxin of the Bacillus Tetani, Science **79**:63-70 and 121-129, 1934. (*b*) Abel, J. J.; Evans, E. A., Jr.; Hampil, B., and Lee, F. C.: Researches on Tetanus: II. The Toxin of the Bacillus Tetani Is Not Transported

*(Footnote continued on next page)*

lymphatics but arrives there only by way of the blood stream. The central action in the spinal cord is one of reflex spasms, as seen in cases of tetanus descendens.[6e] Besides this action there is a definite peripheral effect, causing rigidity of the muscles which are in direct contact with the toxin, either from disturbance of the end plates of the motor nerves or from disturbance of the muscles themselves. This local tetanus has been well described clinically and reproduced experimentally by Ranson.[5c] One of the best examples of this local effect is cephalic tetanus.

With the present understanding of the pathologic physiology of tetanus, the course of events in the case reported may be interpreted as follows: After the initial injury to the right nasolabial fold there was swelling of the right side of the face. Two days later definite paresis of the right side of the face was noted. This interval is much shorter than the usual incubation period of tetanus. On the fourth or fifth day, however, definite trismus appeared, with contraction of the opposite facial muscles, which is in keeping with the expected time of onset of local tetanus. Owing either to the small amount of toxin produced or to the effective action of the antitoxin, or to both, neither tetanus descendens nor local rigidity of the pharyngeal muscles developed. The patient obviously had a fairly mild infection with gradual complete subsidence of symptoms. In spite of the favorable course of the disease, however, there was flaccid paralysis of the right side of the face, as evidenced by careful clinical examination and electrical tests. This would seem hard to explain on the basis of an overwhelming amount of toxin producing paralysis of central origin, since in such a case a more serious outcome was to be expected; nor can the condition have been of peripheral origin, as it has been shown that the peripheral action of tetanus is muscular rigidity and contracture.[5c]

A most important feature, and one not duplicated in the literature, was the loss of the sense of taste on the anterior portion of the tongue on the right. This loss cannot be anatomically explained by action of the toxin on the motor nucleus of the facial nerve. It is best accounted for by disturbance of the chorda tympani in its passage with the facial nerve through the facial canal in the temporal bone. It seems reasonable to postulate edema and compression of the nerves at this

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to the Central Nervous System by Any Component of the Peripheral Nerve Trunks, Bull. Johns Hopkins Hosp. **56**:84-114, 1935. (*c*) Abel, J. J.; Hampil, B., and August, A. F.: Researches on Tetanus: III. Further Experiments to Prove That Tetanus Toxin Is Not Carried in Peripheral Nerves to the Central Nervous System, ibid. **56**:317-336, 1935. (*d*) Abel, J. J.; Evans, E. A., Jr., and Hampil, B.: Researches on Tetanus: V. Distribution and Fate of Tetanus Toxin in the Body, ibid. **59**:307-391, 1936. (e) Firor, W. M., and Jonas, A. F., Jr.: Researches on Tetanus: VI. The Production of Reflex Motor Tetanus by Intraspinal Injections of Tetanus Toxin, ibid. **62**:91-109, 1938. (*f*) Abel, J. J.; Hampil, B.; Jonas, A. F., Jr., and Chalian, W.: Researches on Tetanus: VII. (1) The Time Required for the Fixation of a Fatal Quantity of Tetanus Toxin; (2) The Return Passage of Toxin by Way of the Lymphatic Capillaries to the Cardiovascular System; (3) The Return Passage as a Basis of a Method for the Approximate Determination of the Volume of Lymph in the Closed Lymphatic System, ibid. **62**:522-563, 1938. (*g*) Abel, J. J., and Chalian, W.: Researches on Tetanus: VIII. At What Point in the Course of Tetanus Does Antitetanic Serum Fail to Save Life? ibid. **62**:610-633, 1938.

point, particularly in the presence of facial swelling and some degree of cellulitis. This mechanism is that usually ascribed to Bell's palsy and anatomically seems tenable in this instance. The further clinical course, with recovery within six weeks, also corresponds to the course of Bell's palsy when complete degenerative reaction does not occur.

The failure of facial contraction to develop on the right side was probably due to injury of the facial nerve by edema and inflammation during the incubation period, for it is well known experimentally that local tetanus does not develop unless the motor nerve is intact.[5e]

The trismus and contraction of the muscles of the left side of the face represent the characteristic action of the tetanus toxin. Most of the toxin produced was fixed by these muscles, or that reaching the central nervous system from the blood stream was neutralized by the antitoxin during the longer incubation period of tetanus descendens, as general tetanus never appeared.

## SUMMARY AND CONCLUSIONS

A case of cephalic tetanus with recovery is reported.

An undoubtedly peripheral type of facial paralysis on the side on which the wound was present was observed, with altered electrical responses and recovery in six weeks.

Gustatory sensation on the same side of the tongue anteriorly was diminished with subsequent return to normal.

It is concluded from these observations, in the light of present knowledge of tetanus, that the facial paralysis and loss of gustatory sensation accompanying cephalic tetanus are not due to the specific action of tetanus toxin on the central nuclei or motor end plates, as was previously supposed. Anatomically and clinically these conditions correspond with those observed in Bell's type of facial palsy.

# RAPIDLY FATAL PONTILE HEMORRHAGE

## Clinical and Anatomic Report

STEPHEN KÖRNYEY, M.D., SZEGED, HUNGARY

Von Monakow,[1] on the basis of the material of Durand-Fardel, stated that 10 per cent of all cerebral hemorrhages occur in the pons. From his description, however, it is not certain that he considered as pontile hemorrhages only those which occurred without evidence of additional hemorrhage within the brain. The more recent statistics of Novák [2] showed an exclusively pontile location of 5 per cent of 938 cerebral hemorrhages verified by medicolegal autopsy.

Luce,[3] Böhne [4] and Neubürger [5] stated that the tegmentum is relatively often the seat of massive hemorrhage. Several authors (Gowers [6] and Luce) have maintained that pontile hemorrhage, while often located close to the midline, usually does not cross the median raphe. Most descriptions of pontile hemorrhage have been those of syndromes caused by unilateral pontotegmental lesions. Oppenheim,[7] however, stated that bilateral involvement of the extremities and cranial nerves in cases of pontile hemorrhage is fairly common.

The symptoms of pontile hemorrhage are usually so fulminating and fatal termination is so rapid that analysis of neurologic signs and symptoms has usually been impossible. In the case here reported the rare opportunity was given to observe the development of the clinical signs and symptoms from their onset. Thus, an interesting clinical syndrome could be correlated with the observations at autopsy.

### REPORT OF CASE

*History.*—O. H., a printer aged 39, was first seen in the surgical clinic of the University Hospital on June 4, 1937, at 4 p. m., a few minutes after the completion of an electrocardiogram. A letter from the home physician stated that the patient was suffering from malignant hypertension and that he was sent for the consideration of operative treatment.

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From the Division of Neurosurgery and the Neuropathological Laboratories of the University of Michigan. This work was carried out while I held a fellowship of the Rockefeller Foundation.

1. von Monakow, C.: Die Gehirnpathologie, Vienna, A. Hölder, 1897, p. 765; ed. 2, 1905, p. 1181.

2. Novák, E.: Orvosi hetil. **72**:1151, 1928.

3. Luce, H.: Zum Kapitel der Ponshämorrhagien, Deutsche Ztschr. f. Nervenh. **15**:344, 1899.

4. Böhne, C.: Kompakte apoplektische Hirnblutung und hämorrhagische Hirnerweichung, Ztschr. f. klin. Med. **117**:31, 1931.

5. Neubürger, K.: Anatomische Betrachtungen zur Pathogenese der sanguinösen Apoplexie, Deutsche med. Wchnschr. **58**:690, 1932.

6. Gowers, W. R.: A Manual of Diseases of the Nervous System, London, J. & A. Churchill, 1888, vol. 2, p. 362.

7. Oppenheim, H.: Textbook of Nervous Diseases, translated by A. Bruce, New York, O. Schulze & Co., 1911, p. 804.

While the routine history was being taken the patient commenced to complain of generalized weakness and dizziness. He stated that he had noted numbness and tingling of the hands just before he left the station at which his heart had been examined. As the taking of the history continued he became extremely restless and apprehensive. He complained of inability to hear, difficulty in swallowing and dyspnea. The patient was placed on the examining table and the blood pressure was found to be 245 systolic and 170 diastolic.

Under the eyes of several examiners complete bilateral palsy of the sixth nerve developed; both pupils dilated, and the corneal reflexes disappeared. The patient was still able to talk, but with a typical bulbar speech, and seemed almost totally deaf. The left leg now became paretic, rapid clonic movements being observed. The Babinski sign was present bilaterally.

By 4:15 the patient was completely stuporous, and the blood pressure had risen to 280 systolic and 170 diastolic. This rapidly progressive chain of events was most unpleasant to witness and produced a depressing effect on the nurses and physicians.

The patient was admitted to the medical ward at 4:30.

*Examination.*—The patient was well developed and nourished and almost completely stuporous. Vomiting of the projectile type was present. Respiration was stertorous and of cogwheel type; the rate was 24. The pulse rate was 120. There was slight cyanosis of the nail beds. The skin was warm, soft and dry.

There was miosis and the pupils reacted to light. Both eyes were in convergence. The fundi showed marked hypertensive retinitis, with a large hemorrhage in the left fundus. There was apparent paralysis of the motor roots of both fifth nerves, as the jaw drooped. There seemed to be bilateral palsy of the facial nerve from the appearance of the angles of the mouth and symmetric ballooning of the cheeks on expiration.

Examination of the lungs revealed a few moist rales at the bases. The left border of cardiac dulness was 10 cm. to the left of the midsternal line in the fifth intercostal space. The apical impulse was of moderate intensity, 10 cm. from the midsternal line. The rhythm was regular. No murmurs were heard. The aortic second sound was accentuated. The blood pressure was 300 systolic and 190 diastolic. The peripheral vessels were not remarkable. The abdomen seemed grossly normal when palpated.

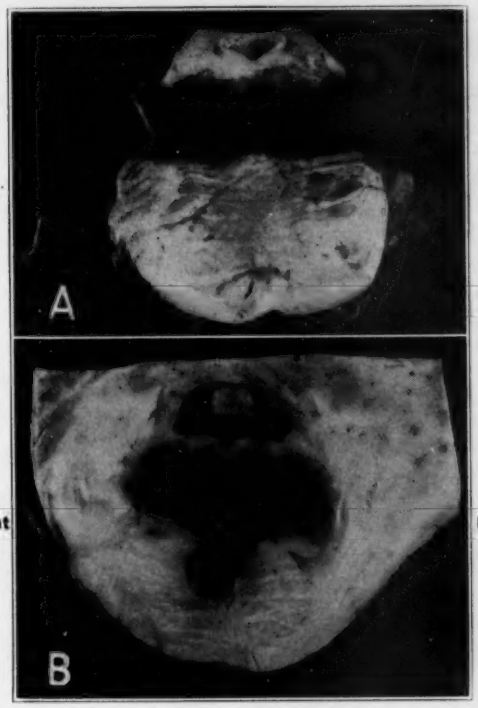
Both tonic and clonic convulsive movements of all extremities were noted. All deep reflexes were markedly exaggerated. The Babinski sign was present bilaterally, and there was bilateral ankle clonus.

A review of the laboratory data obtained the previous day and the electrocardiogram taken just prior to the cerebral accident showed the following picture: There was 28.5 mg. of nonprotein nitrogen per hundred cubic centimeters of blood. The Kahn test was negative. Roentgen examination of the chest showed moderate generalized cardiac enlargement with relative enlargement of the left ventricle, calcifications in the peribronchial nodes and pulmonary parenchyma. The electrocardiogram showed a cardiac rate of 95; sharply inverted T waves in leads I and II, with a large QRS group in lead II, and frequent ventricular extrasystoles. The curve suggested myocardial changes.

*Course in the Hospital.*—Venisection was performed and approximately 750 cc. of blood was removed. The blood pressure was 290 systolic and 140 diastolic after the venisection. Soluble phenobarbital U. S. P. (sodium phenobarbital), 4 grains (0.26 Gm.), was given intramuscularly. By 5:45 p. m. the convulsive movements

had lessened markedly. There was no further vomiting. The pulse was of good quality, but rapid. Respirations were as before. At 6 p. m. the patient gasped deeply once, and respirations immediately ceased. The pulse ceased approximately thirty seconds after this.

*Autopsy.*—This was performed at 9 p. m. on June 4, 1937. The pathologic diagnosis was marked cardiac hypertrophy; coronary sclerosis, with multiple old infarctions of the left ventricle; endocardial sclerosis; atherosclerosis of the aortic valve, aorta and large branches; arteriosclerotic nephropathy; organized thrombosis of a branch of the pancreatic artery; chronic passive congestion of all organs; old tubercles, with recent miliary spread in the lungs, bronchial nodes, liver and spleen; old adhesions of the left pleura, and adenomatous thyroid.




*A*, appearance of the hemorrhage at the level of the posterior colliculi. *B*, cross section of the pons about the level of the sixth nerves. The massive tegmental hemorrhage and the smaller hemorrhages in the basilar part may be seen.

In the brain, the basal vessels showed arteriosclerosis. There was no external evidence of rupture. There was marked edema. The leptomeninges were markedly thickened and edematous. The ventricular fluid was clear. The basal sinuses contained little fluid blood.

Gross frontal sections revealed that the hemorrhage extended caudo-orally from the limit between the medulla oblongata and the pons up to the level of the posterior colliculi (fig., *A*). In the caudal part of the pons (fig., *B*) its transverse axis reached the ventrolateral edge of the tegmentum on each side. Its ventral

borderline corresponded fairly well with the limit between the tegmentum and the basal part, but extended a little into the latter. Dorsally a strip about 0.5 cm. high under the fovea rhomboidea and the quadrigeminal plate escaped destruction. About 0.5 cm. cephalad to the plane shown at *A* in the figure, corresponding to the border between the pedunculi and the pons, the most superior extension of the hemorrhage appeared as a triangular hemorrhagic area in each ventrolateral angle of the tegmentum. Besides this massive hemorrhage others were seen in the basilar part of the pons, one pea-sized to the right of the midline, and several about the size of a pinhead in the midline. In microscopic sections one could trace caudally a confluence of these small hemorrhages and their extension into the left half of the basilar part.

Histologic Observations: In Nissl preparations in the greater part of the hemorrhagic areas both ganglion cells and glia nuclei were preserved. The ganglion cells in these fields, of course, had suffered more or less marked pathologic changes. The glia cells seemed to lie farther apart than in normal tissue. There seemed, consequently, to be much less destruction of nerve tissue than distention of its elements, caused by the imbibition of blood. Whether there was real destruction in the central part of the massive tegmental hemorrhage was uncertain, since, on account of its friability, there was the possibility of some loss of tissue in the course of the microtechnical preparation. Several small perivascular hemorrhages lay around the medial vessels of the tegmentum up to the fovea rhomboidea, especially in the caudal levels. The subarachnoid space in some places around the pons contained a minimal amount of fresh blood, and a thin layer of erythrocytes seemed to adhere to the floor of the fourth ventricle. In the area of the large hemorrhage extensive collections of polymorphonuclear leukocytes were seen, sometimes in or around necrotic vessel walls. Independent of the fresh hemorrhage, a small focus of softening could be recognized, in the stage of scavenger cell decomposition, at the level shown at *A* in the figure.

Pathologic changes of the blood vessels were present both inside and outside the hemorrhagic areas. The basilar artery showed marked sclerosis; some intrapontile and cerebellar vessels revealed more or less marked hyalinization of the media, endothelial or adventitial proliferation or typical sclerotic changes in all layers of their walls. A few intrapontile vessels were surrounded by lymphocytic infiltrate, and some of them, mainly in the basilar part, by glial proliferation.

Within the area of the larger hemorrhages many of the blood vessels showed necrotic changes of their walls, as described in apoplexy by Rosenblath [8] and Westphal and Bär,[9] in fresh traumatic lesions by Staemmler [10] and Wolff [11] and as a consequence of experimental injection of blood into the brain in animals by Hiller.[12] These "angionecrotic changes" were restricted to the massive hemor-

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8. Rosenblath: Ueber die Entstehung der Hirnblutung bei dem Schlaganfall, Deutsche Ztschr. f. Nervenh. **61**:10, 1918.

9. Westphal, K., and Bär, R.: Ueber die Entstehung des Schlaganfalles, Deutsches Arch. f. klin. Med. **151**:1, 1926.

10. Staemmler, M.: Ueber Veränderungen der kleinen Hirngefässe in apoplektischen und traumatischen Erweichungsherden und ihre Beziehungen zur traumatischen Spätapoplexie, Beitr. z. path. Anat. u. z. allg. Path. **78**:408, 1927.

11. Wolff, K.: Grundlagen zu dem Problem der spontanen apoplektischen Hirnblutungen, Beitr. z. path. Anat. u. z. allg. Path. **89**:249, 1932.

12. Hiller, F.: Zur Pathogenese der apoplektischen Hirnblutung, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **42**:202, 1930.

rhage, being absent in the small perivascular extravasations in the dorsal part of the tegmentum.

In Nissl sections of the frontal cortex, insula, cornu ammonis, thalamus, red nucleus and substantia nigra no definite pathologic changes were present.

## COMMENT

The following tabulation shows the complete correlation between clinical symptoms and the extension of the hemorrhage over the areas of the tegmentum. Stress is to be laid on the practically complete bilateral symmetry of the destruction.

| Clinical Symptoms | Areas Affected |
|---|---|
| Tingling of the hand | Spinobulbothalamic tracts |
| Difficulty in hearing | Terminal nuclei of the cochlear nerve and decussation of the auditory tracts |
| Convergent strabismus | Root of the sixth nerve |
| Facial palsy | Nucleus and root of the seventh nerve |
| Drooping of the jaw and corneal areflexia | Nucleus of the fifth nerve and its descending tract |
| Pupillary changes | Sympathetic pathways in the ventral part of the tegmentum (apparently first stimulated and later paralyzed) |

Tonic-clonic seizures in cases of pontile hemorrhage have been known since the early observations of Gintrac and Nothnagel,[13] various attempts having been made to explain their pathophysiologic mechanism; their occurrence in this case merits attention. Luce [14] emphasized that particularly hemorrhages in the basilar part of the pons are capable of causing convulsions, while stimulation of the tegmentum cannot elicit epileptiform phenomena. However, most of the more recent authors, like Marburg,[15] have not attributed any localizing value to convulsions occurring with pontile apoplexy and have expressed the belief that they are induced by an increase of intracranial pressure by rupture into the ventricular system or by other complications.

It is noteworthy that in this case the convulsions started in the left lower extremity and spread from this to the rest of the musculature. They appeared soon after the onset of the paretic symptoms. The circumscribed beginning of the convulsions gains significance from the fact that a pea-sized hemorrhage was present in the dorsomedial part of the right half of the basilar portion of the pons. According to the evidence in a case of Lhermitte and Trelles,[16] symmetric foci in this

13. Nothnagel, H.: Topische Diagnostik der Gehirnkrankheiten, Berlin, A. Hirschwald, 1879, p. 101.

14. Luce,[8] p. 348.

15. Marburg, O.: Ueber die neueren Fortschritte in der topischen Diagnostik des Pons und der Oblongata, Deutsche Ztschr. f. Nervenh. **41**:41, 1911.

16. Lhermitte, J., and Trelles, J. O.: L'artério-sclérose du tronc basilaire et ses conséquences anatomo-cliniques, Jahrb. f. Psychiat. u. Neurol. **51**:91, 1934.

location are apt to cause paraplegia of the lower extremities; hence, it is reasonable to assume a somatotopic distribution of the fibers in the pontile pyramidal area. The basilar hemorrhage in this case seemed to correspond to the pyramidal fibers of the left lower extremity, which first showed paresis and convulsions. The evidence, therefore, favors explanation of the causation of convulsions with pontile hemorrhage as a result of irritation of the pyramidal fibers in their course through the pons. Neither intracranial pressure nor rupture into the ventricular system, the causes given by Marburg, was likely to have played an important role in this case; the hemorrhage had not burst into the ventricle, and there was no reason to assume an increase in the pressure of the ventricular fluid. At least, in the anatomic preparation the aqueduct was seen to be patent.

Another possible explanation, however, must be admitted. Many observations have indicated that the catastrophe which causes apoplectic hemorrhage can exert at the same time an influence on different parts of the brain and on other organs. This seems to be supported by the presence of multiple hemorrhages, a long known example of which is the simultaneous occurrence of striatal and pontile hemorrhages, especially emphasized by Schwartz,[17] according to whom the crisis in the blood supply, while producing an apoplectic hemorrhage, may cause effects elsewhere which are not necessarily accompanied with extravasation. However, it is difficult to interpret the histologic changes outside the main hemorrhagic foci, which at first glance seem to be directly related to the apoplectic hemorrhage. Thus, for instance, the ischemic changes in the ganglion cells in the cornu ammonis, described by Neubürger,[18] can be interpreted as a consequence of a diminished supply of oxygen produced by retardation of the venous flow consequent to increased intracranial pressure. In spite of the many uncertainties in this field, one is at least entitled to assume that in some cases of apoplexy circulatory and nutritive changes outside the territory of the hemorrhage may cause epileptiform discharges. The facts already discussed favor the assumption of a real pontile origin in this case.

The location of the hemorrhage arouses interest from another point of view. Figures 2 and 3 of Böhne's [19] paper on the blood supply of the pons show that the part of the tegmentum involved in this case has a blood supply different from the basal part, the bottom of the fovea rhomboidea and the territory lying ventral and lateral to the aqueduct. The most medial of the so-called rami ad pontem longi at the level of the seventh and the fifth nerve roots enter into the brachium pontis and then, after ascending vertically up to the height of the facial nuclei, swing medially to supply the territory which in this case was destroyed by the massive hemorrhage. The anterior part of this area, lying imme-

17. Schwartz, P.: Die Arten der Schlaganfälle des Gehirns und ihre Entstehung, in Foerster, O., and Wilmanns, K.: Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1930, no. 58.

18. Neubürger, K.: Ueber Ammonshornveränderungen bei apoplektischen Hirnblutungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **111**:325, 1927.

19. Böhne, C.: Ueber die arterielle Versorgung des Gehirns: III. Ueber die arterielle Versorgung des Pons, Ztschr. f. d. ges. Anat. (Abt. 1) **84**:777. 1927.

diately behind the posterior colliculi, is also supplied by long pontile branches. Thus, there were (1) a distribution of the apoplectic hemorrhage strictly corresponding with the terminal territory of small arteries and (2) a symmetric involvement of the same tegmental arterial territory on both sides. The significance of both of these facts has been emphasized by Schwartz, who saw in them proof of the functional genesis of the apoplectic hemorrhage, independent of gross changes in the vessel walls. The small hemorrhages in the basal part seemed to be located in the area of so-called short pontile branches. It is interesting that apparently all arteries ascending through the territory of the large hemorrhage showed the angionecrotic changes previously mentioned, and so did the median branches of the basilar artery. In spite of this, only small perivascular extravasations were present in the terminal distribution—that is, in the tegmentum dorsal to the area of the large hemorrhage.

SUMMARY

A case of pontile hemorrhage is analyzed from clinical and anatomic points of view. Observation of the clinical symptoms and signs from their onset made possible an exact correlation with the anatomic findings. A massive hemorrhage was located symmetrically in the ventral part of the tegmentum. Its location from the caudal border of the pons up to the level of the posterior colliculi corresponded to the area irrigated by the so-called rami ad pontem longi of the basilar artery. This symmetric situation of the hemorrhage in the terminal territory of certain arteries is in accordance with the theory of functional genesis of cerebral apoplexy. An analysis of this case favors the local genesis of epileptiform convulsions observed in some cases of pontile hemorrhage.

# ARGYLL ROBERTSON PUPILS IN ALCOHOLISM

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NEW YORK

That the Argyll Robertson pupil may occur in nonsyphilitic disease of the central nervous system is not well appreciated in clinical medicine. Ordinarily, one associates such a pupillary reaction with tabes or dementia paralytica. However, it is important to bear in mind other conditions in which this pupillary reaction may occur, infrequent though it may be. Cases have been reported in which an Argyll Robertson pupil has been observed in association with multiple sclerosis;[1] meningitis;[2] wood alcohol poisoning;[3] arteriosclerosis;[4] encephalitis;[5] diabetes,[6] and tumors of the pituitary gland,[7] pons[8] and colliculi.[9]

Argyll Robertson[10] described the characteristic pupil as miotic, not responding to light but reacting normally to stimuli of accommodation and convergence, and of irregular outline, with little or no response to mydriatic drugs or psychogenic stimuli.

Moore[11] stated that in cases of nonsyphilitic conditions the pupil has special characteristics: The light reflex is absent; the accommodation-convergence reflex is present, but is less marked than normal and is difficult to elicit because of the small excursion; the Argyll Robertson pupil is likely to be unilateral; the pupil dilates to mydriatic drugs, but sluggishly, and is usually not contracted, as is generally true in cases of tabes.

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From the Department of Psychiatry, the New York University College of Medicine, and the Psychiatric Division of the Bellevue Hospital.

1. Wechsler, I. S.: A Textbook of Clinical Neurology, ed. 3, Philadelphia, W. B. Saunders Company, 1935, p. 74.

2. Terrien and Dupuy-Dutemps, P.: Paralysie progressive du III, du IV, du V et du VI gauches avec signe d'A. Robertson homolatéral, Ann. d'ocul. **170**: 250 (March) 1933.

3. Fuchs, cited by LeFever.[7]

4. Woltman, H. W.: Arteriosclerosis of the Nervous System: An Analysis of Fifty-Nine Cases with Cord Changes, M. Clin. North America **5**:511 (Sept.) 1921.

5. Wechsler,[1] p. 391.

6. Jordan, W. R.: Neuritic Manifestations in Diabetes Mellitus, Arch. Int. Med. **57**:307 (Feb.) 1936. Wakefield, E. G.: Diabetic Neuritis, Proc. Staff Meet., Mayo Clin. **3**:256 (Aug. 29) 1928.

7. LeFever, C. W.: Argyll Robertson Syndrome Occurring with Pituitary Tumors: Report of Two Cases, Am. J. Ophth. **18**:442 (May) 1935.

8. Wechsler,[1] p. 423.

9. Wechsler,[1] p. 411.

10. Argyll Robertson, D., cited by Merritt, and Moore.[12]

11. Moore, R. F.: The Non-Luetic Argyll-Robertson Pupil, Tr. Ophth. Soc. U. Kingdom **51**:203, 1931.

Even in cases of syphilis various types of pupils may be found. Spiller pointed out that the Argyll Robertson pupil is necessarily of gradual development and may occur in one eye before it does in the other. Hence, one may find mydriasis instead of miosis or inequality of the pupils.

It is not my purpose to discuss the theories relative to location of the lesion producing the Argyll Robertson pupil. These have been well covered in recent contributions to the literature by Merritt and Moore,[12] Ranson and Magoun[13] and Harris.[14]

From the standpoint of clinical diagnosis, it is well to report cases in which an Argyll Robertson pupil of nonsyphilitic origin occurs. A proper diagnosis is important to the patient as well as to diagnostic acumen.

That pupillary changes occur in chronic alcoholism is well known. These are more likely to be associated with peripheral neuritis or toxic amblyopia. One may find the pupils dilated and fixed both to light and in accommodation; they may be only sluggish in reaction and are frequently of unequal size. A true Argyll Robertson pupil is rare, but may occur.

From the psychiatric division of the Bellevue Hospital, where there are admitted from 10,000 to 12,000 alcoholic patients every year, personal examination revealed only 3 cases in the group for one year.

## REPORT OF CASES

CASE 1.—*History.*—V. H., a white man aged 45, was admitted from the municipal lodging house, where it was stated that he had been disoriented and confused. The history, given by the patient, was that he had been addicted to alcohol for many years and had recently been on a prolonged spree. He said he had never had a chancre or any illnesses requiring treatment by injections. He stated that he had been married and had three children, but had been separated from his family for many years.

*Physical Examination.*—The pupils were constricted, irregular and fixed to light, but reacted well in accommodation. The fundi and movements of the eyeballs were normal. Neurologic examination otherwise gave insignificant results except for the presence of mild peripheral neuritis in the legs, as shown by diminished ankle jerks and hyperesthesia of the feet. In addition, there was a healing pellagrous lesion on the back of each hand.

*Psychiatric Examination.*—There were disorientation, memory defects and confabulations—a picture typical of the Korsakoff psychosis.

*Laboratory Findings.*—The Wassermann reaction of the blood was negative. Examination of the spinal fluid revealed no globulin, 2 cells per cubic millimeter, a negative Wassermann reaction and a colloidal gold curve of 0000000000.

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12. Merritt, H. H., and Moore, M.: The Argyll Robertson Pupil: An Anatomic-Physiologic Explanation of the Phenomenon, with a Survey of Its Occurrence in Neurosyphilis, Arch. Neurol. & Psychiat. **30**:357 (Aug.) 1933.

13. Ranson, S. W., and Magoun, H. W.: The Central Path of the Pupilloconstrictor Reflex in Response to Light, Arch. Neurol. & Psychiat. **30**:1193 (Dec.) 1933.

14. Harris, W.: The Fibers of the Pupillary Reflex and the Argyll Robertson Pupil, Arch. Neurol. & Psychiat. **34**:1195 (Dec.) 1935.

CASE 2.—*History.*—B. K., a white man aged 31, was admitted from the clinic because of acute alcoholism. He had been attending the clinic for almost a year for treatment of pains in the legs due to peripheral neuritis. He had had alcoholism for many years, but there was no history of venereal disease. He was aware that something was wrong with the pupils of his eyes because in the clinic he had been questioned closely about syphilis and an examination of the spinal fluid and a provocative Wassermann test had been made.

*Physical Examination.*—The patient was healthy in appearance, and general physical examination revealed nothing abnormal. The pupils were equally miotic, irregular and fixed to light on the two sides, but reacted in accommodation. There was slight response to mydriatics. The fundi and movements of the eyeballs were normal. The rest of the neurologic examination revealed nothing abnormal except peripheral neuritis in the lower extremities. The ankle jerks were absent. There was hypesthesia up to the lower part of the thighs, where there was a band of hyperesthesia. The patient complained of shooting pains and burning in the feet. There was mild weakness of the legs.

*Psychiatric Examination.*—There were no defects in orientation or memory and no evidence of psychotic disorder.

*Laboratory Examination.*—The Wassermann reaction of the blood was negative, even after a provocative injection. The spinal fluid contained no cells; tests for globulin and the Wassermann test gave negative results. The colloidal gold curve was flat.

CASE 3.—*History.*—E. F., a white man aged 62, was admitted from his residence, where he had been in delirium. He was a widower, with two married daughters. There was a history of heavy drinking throughout his life, this being his second attack of delirium tremens. There was no history of venereal disease.

*Psychiatric Examination.*—The patient remained in delirium for two days after his admission. He was fearful and expressed the delusion that men were coming through the window to kill him. He was confused and responded to hallucinations.

*Physical Examination.*—There was mild arteriosclerosis of the peripheral vessels. The blood pressure was 150 systolic and 90 diastolic. The pupils were small, regular and fixed to light, but reacted in accommodation. The fundi and movements of the eyes were normal. Neurologic examination otherwise gave normal results.

*Laboratory Examination.*—The Wassermann reaction of the blood was negative. Examination of the spinal fluid showed no globulin, 4 cells per cubic millimeter, a negative Wassermann reaction and a normal colloidal gold curve.

*Course.*—The patient recovered from his delirium and within a few days showed normal mentality. Reexamination of the pupils at this time showed a marked change. They were now equal and of normal size and reacted well both to light and in accommodation.

## SUMMARY AND COMMENT

These 3 cases illustrate the association of an Argyll Robertson pupil with chronic alcoholism. In case 1 there was evidence of widespread damage to the central nervous system, as shown by the Korsakoff type of mental change, the peripheral neuritis and the pellagrous lesion. In case 2 the classic pupillary change was found, together with extensive

peripheral neuritis in the legs. In case 3 there was a transitory pupillary reaction of the Argyll Robertson type during the course of delirium tremens. Wherever the pathologic lesion that is responsible for an Argyll Robertson pupil exists in cases of neurosyphilis, it seems that a similar pupillary change may be produced in other conditions. In cases of chronic alcoholism the Argyll Robertson pupil was found accompanying other neurologic disturbances. It is interesting to note that this manifestation may be transitory, as in case 3. Possibly, with repeated attacks a permanent pupillary change may result.

## CONCLUSION

The literature on the Argyll Robertson pupil of nonsyphilitic origin has been briefly reviewed and its clinical importance pointed out. Three cases of chronic alcoholism in which Argyll Robertson pupils were found have been reported.

# HAVELOCK ELLIS

## AN APPRECIATION

Havelock Ellis was born eighty years ago, on Feb. 2, 1859, in Surrey, England, the son of a British seaman, and the last of a long line of English clergymen, mariners and merchants. Though Ellis is known for the wide range of his culture and interests, for his distinction as critic and writer, for his rare personal charm and for his broad humanity, he will perhaps be best and longest remembered for the work to which at an early age he had dedicated his life and energy—that of bringing human sex psychology within the scope of science. His seven monumental volumes of "Studies in the Psychology of Sex" have probably served more than any other single work to bring sex out of the atmosphere of ignorance and prudery into the clear light of science, and will always remain an incomparable critical digest of the scientific knowledge of the subject up to contemporary times.

The scientific study of sex is nowadays accepted almost without question, but the destruction of the old taboos and prejudices was not accomplished without hardship and sacrifice. The appearance of Ellis' first volume of the "Studies," in 1897, was followed by a prosecution for the distribution of what the judge described as a "filthy publication." The sale of the book was suspended in England, but it is a matter of pride to American scientists that the "Studies" could thereafter be published in this country. "I am a student," wrote Ellis in his memorable "Note on the Bedborough Trial," "and my path has long been marked out. I may be forced to pursue it under unfavorable conditions, but I do not intend that any consideration shall induce me to swerve from it." His life achievement is the best testimony to the success of this early resolve.

We hope that Havelock Ellis will for many years continue to exercise his great and good influence. His life and work remain an inspiration not only to us but to future generations as well.

John Dewey
Adolf Meyer
Bertrand Russell
Margaret Sanger
Bronislaw Malinowski
Henry E. Sigerist
Houston Peterson
D. L. Dickinson
Irwin Edman

# News and Comment

## RESIDENCY IN NEUROLOGY

A residency in neurology of one year's duration is available at the Jefferson Medical College Hospital, in Philadelphia. The service comprises 25 beds, with a rapid turnover of all types of acute neurologic conditions. Neurosurgical training is also available, as well as training in neuroanatomy and neuropathology. Applications should be addressed to Dr. Bernard J. Alpers, 111 North Forty-Ninth Street, Philadelphia.

## ASSOCIATION MEETINGS

American Psychiatric Association, Palmer House, Chicago, May 8 to 12, 1939.

American Psychoanalytic Association, Palmer House, Chicago, May 8 to 11, 1939.

American Association on Mental Deficiency, Palmer House, Chicago, May 3 to 6, 1939.

American Association of Industrial Physicians and Surgeons, Hotel Statler, Cleveland, June 5 to 8, 1939.

American Neurological Association, Ambassador Hotel, Atlantic City, N. J., June 5 to 7, 1939.

## THOMAS W. SALMON MEMORIAL LECTURES

The Salmon Committee on Psychiatry and Mental Hygiene announces the seventh series of Thomas W. Salmon Memorial Lectures, to be given by Dr. Edward A. Strecker, chairman of the department of psychiatry of the University of Pennsylvania, on successive Friday evenings, April 14, 21 and 28, at 8:30 p. m., at the New York Academy of Medicine, 2 East One Hundred and Third Street, New York.

Dr. Strecker's lectures, entitled "Beyond Clinical Frontiers," will be divided into three sections: On April 14 he will discuss "The Massive Retreat from Reality"; on April 21, "Crowd Mindedness," and on April 28, "Threats to Our Culture."

Dr. Strecker will give a résumé of his lectures in Toronto, Canada, on the evening of May 5, at the Academy of Medicine.

Members of the medical profession and their friends are cordially invited to attend the lectures at the New York Academy of Medicine or to hear Dr. Strecker in Toronto.

# Obituaries

## MILTON MORRIS ABELES, M.D.
1906–1938

Finally to recite the memorial for a beloved friend, comrade and colleague is to admit his death into the scheme of things. This is perhaps the reason that these inadequate words, written with reluctant submission, have been delayed. In a shocking accident on Aug. 13, 1938, Dr. Abeles and his bride of three weeks died when their plane, en route from Prague to Strasbourg, crashed against a mountain peak of the Black Forest, in Germany.

Milton Morris Abeles was born on March 4, 1906. Educated in the public schools of New York, he entered the New York University College of Medicine in 1930. He interned at the Montefiore Hospital of New York and became the resident neurologist of that institution, in the service of Dr. S. P. Goodhart. From July 1, 1933 to his death he served the city of New York, first as assistant alienist, then as alienist, in the psychiatric division of the Bellevue Hospital. In 1935 he was elected a member of the New York Society for Clinical Psychiatry. At about that time he was appointed assistant in neurology at Columbia University. His thorough training and unexcelled performance as alienist in charge of the prison ward of the psychiatric division won him appointment to the teaching staff of the New York University College of Medicine, as an instructor in psychiatry.

This simple enumeration of his achievements in laying the foundation for what promised to be a career of steady progress gives little indication of the things that endeared him to his associates. It was not merely his characteristic adherence to his responsiblities (which earned the respect of his superiors in office) or his wide interests in his science (he had already published original papers in neurology and psychiatry). It was rather that he was one of those rare men whose modesty and kindness exceeded even their great capacity and versatility. He was an artist instinctively: The delicacy of his etchings and paintings was reflected in the more mature precision of his neurologic and ophthalmologic examination and diagnosis.

Most of all, he was loved because one felt secure in his quiet presence. His sense of humor was bright and subtle. He knew how to laugh and, more important, when not to laugh. He knew how to give and when not to take. He was the best of comrades. Though he is gone from our external perspective, he is present to our inner sight, among our most refreshing, life-loving memories, gathered in spite of a hazardous world.

DANIEL E. SCHNEIDER, M.D.

# Abstracts from Current Literature

## Anatomy and Embryology

THE CHANGES IN THE CENTRAL NERVOUS SYSTEM DURING THE LIFE HISTORY OF THE BEETLE PASSALUS CORNUTUS FABRICIUS. FRANCES PERLE CODY and I. E. GRAY, J. Morphol. **62**:503 (May) 1938.

In insects the brain and subesophageal ganglion originate from six cephalic neuromeres, and the other ganglia, from three thoracic and from nine to eleven abdominal neuromeres. During the life history the ganglia undergo various degrees of fusion, concentration beginning in the earliest embryonic stages. This process was studied in Passalus cornutus Fabricius, a large, wood-boring, lamellicorn beetle. In the early embryo there is one ganglion for each body segment: two cephalic, three thoracic and ten abdominal ganglia. The number of thoracic ganglia remains constant throughout the life history. The eighth, ninth and tenth abdominal ganglia coalesce in the early embryo, but only minor changes, such as shortening of connectives, occur in the three larval instars. Between the first and the third day of pupation the nervous system assumes practically the adult form, all the abdominal ganglia fusing into a single mass. Connectives disappear between the mesothoracic and the metathoracic ganglia and between the metathoracic and the abdominal ganglia. Except for the brain and the subesophageal and prothoracic ganglia, the entire ventral nerve chain comes to lie in the mesothorax. In spite of these changes, the peripheral nerves still supply the same segments in which they were originally located and still arise from the ganglia and ganglionic mass in the same relative positions. It is probable, therefore, that the abdominal ganglia do not atrophy but that they become fused into a compact mass. With regard to the modifications of the nervous system occurring during development, Passalus occupies an intermediate position between the more generalized insects, such as the cockroach, and the higher orders, such as certain diptera.

WYMAN, Boston.

THE OPTIC CHIASM IN A CASE OF A PERSON WITH ONE EYE. P. QUERCY and R. DE LACHAUD, Encéphale **1**:73, 1938.

Quercy and de Lachaud examined by serial sections the optic nerves, chiasm and tracts in a patient seven years after enucleation of the right eye. In the optic tract, no distinct temporal and nasal bundles of fibers were observed. Both the direct and the crossed portions of the tract spread out so as to lie in all parts of the tract.

LIBER, New York.

CENTRAL TEGMENTAL BUNDLE AND ITS IMPORTANCE IN THE EXTRAPYRAMIDAL MOTOR SYSTEM. E. WEISSCHEDEL, Arch. f. Psychiat. **107**:443 (Dec.) 1937.

The material used in this study consisted of neurologically normal psychiatric patients, ranging in age from 19 to 49 years. Serial sections of the brains were stained by the Kultschitzky-Wolters method. In addition, the brain of an executed criminal, aged 25, was serially sectioned and stained by the Nissl method. Finally, a number of sections were also stained by the Spielmeyer, Bielschowsky and Holzer methods. The results are summarized. The central tegmental bundle is a complex system consisting of a number of separate tracts which come from different nuclei and lead to specific end stations. The major portion of the tract comes from the red nucleus, most of the fibers originating in the dorsomedial margin of this nucleus. A smaller portion of the tract comes from the globus

pallidus and reaches the red nucleus through the fasciculus lenticularis. Caudal to the red nucleus the fibers cross the brachium conjunctivum and form a large uniform tract in the oral half of the pons. This tract then divides into three parts within the pons: ventral, medial and dorsal.

In the midbrain the central tegmental bundle consists of the following tracts: (1) the rubro-olivary and pallido-olivary tracts, both of which run in the ventral portion of the midbrain and lead to the lower portion of the olive, and (2) the rubroreticular and pallidoreticular tracts, which consist of shorter fibers and lead into the midbrain, pons and medulla. These are gradually replaced by the following reticulofugal tracts: (*a*) the reticulospinal tract, which apparently carries impulses to the whole column of the anterior horn; (*b*) the reticulo-olivary tract, which leads to the lower part of the olive, and (*c*) the reticuloreticular fibers.

The entire system of the central tegmental bundle has as its function the transmission of efferent stimuli from the higher extrapyramidal motor centers to the peripheral motor neurons. In man it is by far the most important carrier of these impulses; the rubrospinal tract has a comparatively accessory extrapyramidal function.

W. MALAMUD, Iowa City.

NUMBER OF NERVE FIBERS IN THE SPINAL ROOTS OF MACACUS RHESUS. A. Y. LARSSON, Upsala läkaref. förh. **43**:139 (May) 1938.

This investigation was undertaken to determine the number of nerve fibers in the spinal roots in Macacus rhesus and to ascertain the ratio between the fibers of the anterior and those of the posterior roots. The observations were then compared with those already established for other animals and for man, and an attempt was made to give the figures a phylogenetic interpretation. A count of the fibers in the sections gave the following figures: In the cervical region there were 79,377 fibers in the posterior roots and 21,435 fibers in the ventral roots, with a ratio of 3.71. In the thoracic region there were 52,013 fibers in the dorsal roots and 28,907 fibers in the ventral roots, with a ratio of 1.8. In the lumbar, sacral and coccygeal regions combined, there was a total of 91,399 fibers in the dorsal roots and 34,053 fibers in the ventral roots, with a ratio of 2.68. There was a total of 227,729 fibers in the dorsal roots and 84,395 in the ventral roots, with a ratio of 2.64. These figures were compared with those previously established for other animals and for man. The highest ratio of 4.7 was found in man by Arnell. The next highest ratio, 2.64, was observed in Macacus rhesus, followed in the dog by a ratio of 2.15 (Agduhr), in the cat by a ratio of 1.85 (Kjellgren) and, finally, in the mole by a ratio of 1.21 (Agduhr). In the cervical region the quotient for the monkey is 3.71, while for the dog it is 2.21. The difference in the ratios for the dog and the cat is less pronounced. Larsson further investigated the relation between the number of the sensory nerve fibers and the area of the skin. Using the ratio for the mouse as a unit, he found the number of sensory fibers in the rat to be 2.05, in the cat 2.09, in the dog 1.42, in the monkey 0.8 and in man 4.27. These observations indicate that the greater the surface area of the skin the larger the number of nerve fibers in the dorsal roots.

NOTKIN, Poughkeepsie, N. Y.

## Physiology and Biochemistry

CHANGES IN BLOOD LIPIDS DURING INSULIN TREATMENT OF SCHIZOPHRENIA. LOWELL E. RANDALL, EWEN CAMERON and JOSEPH M. LOONEY, Am. J. M. Sc. **195**:802 (June) 1938.

The authors report on the state of the blood lipids during the course of insulin treatment in 16 cases of schizophrenia, in 5 of which there was a good remission during treatment. The lipid content of the blood was studied before beginning treatment and at intervals of from two weeks to one month during the course

of the treatment. In 14 of the 16 cases an initial significant rise in the amounts of phospholipid, total lipid and total cholesterol occurred, but in 9 of these there was a return to premedication levels as the treatment proceeded. No significant correlations between the clinical condition and the variations in the lipid content of the blood could be recognized. In the 5 cases in which a good remission occurred during the treatment there was a significant rise in blood lipids from the premedication level. The effects of insulin on the postabsorptive level of blood lipids are not marked or consistent. The rise in blood lipid may signify improvement in the general metabolism of the patient and coincides with improvement in the mental state.

MICHAELS, Boston.

THE INFLUENCE OF HYPOGLYCEMIA ON THE SENSITIVITY OF THE CENTRAL NERVOUS SYSTEM TO OXYGEN WANT. ERNEST GELLHORN, R. C. INGRAHAM and L. MOLDAVSKY, J. Neurophysiol. **1**:301 (July) 1938.

The authors tested the relation between hypoglycemia and anoxia, as far as the central nervous system is concerned, by investigating the reaction of the blood pressure in dogs to a given degree of anoxia obtained by inhalation of 6.2 per cent oxygen. It is known that increasing degrees of anoxia produce proportionately greater rises in blood pressure. On this basis, the reaction of the blood pressure to a given concentration of oxygen (6.2 per cent) may be used as an indicator of the degree of oxygen want in the central nervous system. The results of the experiments follow. Insulin, by virtue of the hypoglycemia produced, causes augmentation in the increased response of the blood pressure to a given degree of oxygen deficiency. This effect is a function of the decrease in the level of the blood sugar. This is indicated by: (*a*) the failure of the effect of augmentation to appear in the experiments in which insulin did not significantly alter the level of the blood sugar; (*b*) the observation that the response of the blood pressure to inhalation of 6.2 per cent oxygen varied inversely as the concentration of the blood sugar, and (*c*) the fact that restoration of the blood sugar level after hypoglycemia by the intravenous injection of dextrose diminishes the response of the blood pressure and restores it to normal.

Of the other monosaccharides, fructose is capable, although to a lesser degree than dextrose, of lessening the degree of response of the blood pressure to oxygen deficiency, and galactose fails to bring about such reversal.

The ionic changes in the blood (potassium, calcium and hydrogen) appear to bear no relation to the phenomenon. The potassium:calcium quotient shows random variations. The phosphorus concentration decreases with the fall in blood sugar. The rate of change for phosphorus, however, differs from that for sugar. The response of the blood pressure is dependent on the change in the sugar rather than that in the phosphorus level of the blood.

That the oxidative processes in the brain are diminished in hypoglycemia is further indicated by the fact that inhalation of 6.2 per cent oxygen may induce Cheyne-Stokes breathing when the blood sugar is low, although it fails to do so when the level of the blood sugar is restored by injection of dextrose, levulose or galactose.

The increased response of the blood pressure to gas mixtures deficient in oxygen (6.2 per cent) observed in cases of hypoglycemia is greater than the rise in blood pressure obtained on inhalation of pure nitrogen at normal levels of the blood sugar. This is due to the fact that hypoglycemia, in contrast to the effects of inhalation of nitrogen, reduces the rate of oxidation in the brain more than in other tissues. Therefore a greater reduction in the oxidative metabolism can be achieved and maintained in the brain by combination of the hypoglycemic state and inhalation of 6 per cent oxygen than by inhalation of nitrogen. In the latter case, heart failure develops rapidly, and the blood pressure falls.

ALPERS, Philadelphia.

THE INFLUENCE OF HYPOTHALAMIC STIMULATION OF INTESTINAL ACTIVITY. JULES H. MASSERMAN and E. W. HAERTIG, J. Neurophysiol. **1**:350 (July) 1938.

Masserman and Haertig studied the effects of electrical stimulation of the hypothalamus and of the injection of strychnine into the diencephalon on the motility and blood supply of the small intestine by direct inspection in cats anesthetized with ether and by fluoroscopic examinaiton of recovery preparations. Observations in 14 animals led to the following conclusions: Stimulation of the anterior portion of the hypothalamus of an anesthetized animal with currents too weak to induce typical emotional mimetic responses caused marked pendular movements of loops of the small intestine and, less consistently, segmentation and peristalsis of the intestine. In some animals these stimuli caused the small vessels in the external portion of the intestinal wall to constrict or dilate slightly, but more frequently no change in vasotonicity could be observed. In the recovery preparations segmentation and peristalsis were induced or augmented more consistently than were the pendular movements. Enteromotor effects were also obtained when the dorsal portion of the supramamiliary decussation and the mamillary bodies were stimulated. Inhibition of intestinal motility was induced by the application of strong electrical stimuli anywhere in the hypothalamus and of weak stimuli in the suprachiasmic region or in the ventral portion of the supramamillary decussation. In stimulation of the hypothalamus the degree of intestinal inhibition corresponded to the intensity of the other autonomic and emotional mimetic responses elicited by the stimulus. Injections of from 0.07 to 0.08 mg. of strychnine sulfate per kilogram of body weight into the diencephalon in cats caused either no change in intestinal activity or a slight accentuation of the intestinal movements. However, the injection of larger amounts of strychnine into the diencephalon was followed consistently by spasticity, diminished motility and blanching of the small intestine. Electrical stimulation of the hypothalamus after strychnine had been injected into it revealed inconsistent lowering of thresholds for the diencephalic enteromotor reactions, the degree of intestinal inhibition in general corresponding to the degree of facilitation of the other vegetative and emotional mimetic responses of the animal to hypothalamic stimulation.

ALPERS, Philadelphia.

REFLEX DISCHARGE FROM THE SPINAL CORD OVER THE DORSAL ROOTS. JAN F. TÖNNIES, J. Neurophysiol. **1**:379 (July) 1938.

Tönnies describes the properties of the reflex discharge which takes place over the spinal dorsal roots of the cat after stimulation of the sensory nerves. Observations were made on the saphenous nerve or on the lumbar roots after stimulation of homolateral or contralateral lumbar roots or sensory nerves of the hindlimb. The homolateral reflex produced by a single afferent volley was characterized by an action potential that rose to a peak in one or two milliseconds, then declined along a curve which showed from two to three secondary crests at intervals of from two and a half to three and a half milliseconds. Alpha fibers were involved exclusively in this part of the reflex. When a reflex was produced in the saphenous nerve by a volley of alpha impulses from the saphenous nerve itself, the first reflex wave was followed by a second wave which was separated from it and was carried in delta fibers. The contralateral reflex produced by a single afferent volley was much smaller than the homolateral reflex, but lasted longer. It started gradually and came to a minimum only after from six to twenty milliseconds. The reduced reflex time of the first discharges in the homolateral dorsal root was four + milliseconds and was independent of the strength of the exciting volley. In the contralateral reflex the time was as much as one and a half milliseconds longer. The reflex produced by an afferent volley could be conditioned by a second, appropriately timed afferent volley in the same or another nerve.

Summation, facilitation and inhibition could be demonstrated. A calculation is given indicating that at least 35 per cent of the alpha fibers in the saphenous nerve are accessible to reflex activation.

ALPERS, Philadelphia.

## Neuropathology

CYSTICERCUS CELLULOSAE OF THE BRAIN: REPORT OF TWO AUTOPSIES. C. C. HARE, J. A. M. A. **111**:510 (Aug. 6) 1938.

Not only is Cysticercus cellulosae rare but the lesions it produces are so distributed, and at times so few, that antemortem diagnosis is often extremely difficult. The condition may be revealed only at the necropsy table. The frequency with which cysticerci are observed in the nervous system in persons otherwise infested with the organisms has been reported variously by different authors. Hare reports 2 cases of long-standing cysticercus infestation of the brain. In 1 case the parenchyma, meninges and fourth ventricle of the brain were involved, and in the other there was cysticercosis of the fourth ventricle with accompanying chronic basilar leptomeningitis.

EDITOR'S ABSTRACT.

CELL CHANGES IN SOME OF THE HYPOTHALAMIC NUCLEI IN EXPERIMENTAL FEVER. L. O. MORGAN, J. Neurophysiol. **1**:281 (May) 1938.

Morgan studied the entire brain stem in 15 dogs and 4 rabbits after experimental production of fever by either a hypodermic or an intravenous injection of typhoid or bronchisepticus toxin. Significant cell changes were observed in only three nuclei of the hypothalamus. The nucleus tuberomamillaris was involved in every case. An average of 60 per cent of the cells in this nucleus showed definite chromatolytic change. A variable amount of chromatolysis was observed in the paraventricular nucleus and the basal optic ganglia in 14 of the 19 animals studied. The average proportion of chromatolytic cells in these cases was 15.8 per cent for the paraventricular nucleus and 12.5 per cent for the basal optic ganglia.

ALPERS, Philadelphia.

JUVENILE AMAUROTIC IDIOCY. MAURICE DIDE and LUDO VAN BOGAERT, Rev. neurol. **69**:1, 1938.

Dide and Van Bogaert report on 2 families in which cases of juvenile amaurotic idiocy appeared. In the first, 3 of 7 siblings were affected. No other cases were known in the rest of the family. The second case occurred in an only child. The parents and grandparents presented no evidence of mental disease. Both families were Catholic, of Spanish descent. In the first family, the patients appeared normal until the age of 7 or 8, when diminution of visual acuity occurred. This was followed by mental deterioration. All 3 patients had retinitis pigmentosa, and 2 had cataracts. One had temporal atrophy of the optic disk. Hypokinetic and cerebellar signs were present. The patient in the second family had always been considered mentally deficient. He had typhoid at the age of 10, followed by epileptic seizures, fugues and agitation and further intellectual deterioration. The eyegrounds showed simple atrophy of the disk, but no retinitis pigmentosa. There was a parkinsonian type of gait, with signs of cerebellar involvement. The patient died at the age of 17. The brain weighed 1,183 Gm. The cerebellum and brain stem weighed 89 Gm., which indicated atrophy both absolute and relative. The density of the right hemisphere was 0.992, and that of the left, 0.97 (normal density, 1.05). The putamen was fibrous. The cerebellum presented slight lamellar atrophy. There was moderate diffuse demyelination of the optic nerves and chiasm. The ganglion cells in all parts of the brain presented varying degrees of

lipoid infiltration, as well as safranophilic granulations. In all regions of the cerebral cortex, layers III b, V and VI were the most involved. Next in order of involvement were layers III a and IV; layer II was least involved. In the thalamus, the lesions were particularly severe in the large cells and in the circular hyperchromic formation of the medial nucleus. In the brain stem, the large cells of the red nucleus, the reticulate zone of the substantia nigra, the periretrorubral formation, the interstitial nucleus, the vesicular cells and the locus caeruleus were severely involved and showed diminution of normal pigment. In the cerebellum the Purkinje cells and the dentate nucleus were most involved. In the spinal cord, the most severe lesions were in the anterior horn cells and in Clarke's column. About the affected ganglion cells was intense fibrillar gliosis. Juvenile amaurotic idiocy affects electively the ganglion cells of the nervous system. The mesenchymal elements are spared. The lesions vary in intensity in different regions of the brain in various cases. This explains the clinical disparity of the disease.

LIBER, New York.

HISTOLOGIC CHANGES IN THE BRAIN FOLLOWING INSULIN COMA. F. KOBLER, Arch. f. Psychiat. **107**:688 (March) 1938.

Kobler describes a case of schizophrenia in which the patient was treated by insulin shock and died in a state of deep coma, with severe epileptic convulsions. There were diffuse cellular changes in the brain, a mild glial reaction and some alterations in the blood vessels of the type seen in severe toxemias. To a large extent the cellular pathologic change revealed itself in disintegration of the nucleus with the formation of vacuoles. Kobler believes that changes of this type are definitely associated with the administration of large doses of insulin.

W. MALAMUD, Iowa City.

ENCEPHALITIS FOLLOWING BANG'S DISEASE. S. SCHEIDIGGER and K. STERN, Ztschr. f. d. ges. Neurol. u. Psychiat. **157**:449 (March) 1937.

Scheidigger and Stern report the case of a man aged 34 who died five months after being bitten in the left hand and forearm by a horse. The wounds healed, but enlargement of the glands in the left upper extremity persisted. While suffering from these wounds the patient took care of four cows who had Bang's disease. Two months after the accident he suddenly became ill with chills and fever. There was a positive reaction to the agglutination test for Bang's bacillus in a dilution of 1:800. During the course of this infection signs of ulcerative endocarditis appeared. The patient was known to have had aortic insufficiency since his fifth year, following scarlet fever. Autopsy showed an old lesion of the aortic valve, with fresh vegetations. No organisms could be cultured from the valves, and no granulomatous changes were seen in any of the organs. The brain and meninges showed miliary granulomatous lesions, which were observed especially in the cerebral cortex, pons, olives and region of the cerebellar nuclei. In a few places in the cerebral cortex there was diffuse infiltration of an inflammatory nature. These small granulomas were definitely related to the blood vessels. They were composed of glia cells, especially microglia cells, lymphocytes, plasma cells and fibroblasts. The prominence of the mesenchymal elements in these areas differentiated the nodules from the foci of gliosis usually noted in encephalitis and typhus. They resembled miliary gummas. There was also evidence of diffuse gliosis throughout the brain, especially in the white substance. The ganglion cells did not seem to be seriously involved. Some cells in the pontile nuclei showed severe alterations. A few perivascular hemorrhages were observed in the cerebral cortex.

SAVITSKY, New York.

WERNICKE'S DISEASE (POLIOENCEPHALITIS HAEMORRHAGICA INTERNA) AND CHRONIC GASTRITIS. KARL NEUBÜRGER, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:208 (Oct.) 1937.

Neubürger previously reported 14 cases of Wernicke's disease in which there was no history of alcoholism. In 10 of these there was cancer—in seven cancer of the stomach. In the first series there was 1 case of chronic gastritis. Two new cases of chronic gastritis associated with Wernicke's polioencephalitis haemorrhagica interna are reported. These 3 cases occurred in women, 70, 70 and 78 years of age, respectively, none of whom had a history of alcoholism. The histologic picture in each case consisted of small hemorrhages, degenerative changes in the ganglion cells and alterations in the blood vessels in the periaqueductal region, the mamillary bodies, the quadrigeminal bodies and the thalamus. In 1 case the medial geniculate body was involved. The gastric mucosa in all 7 cases showed marked atrophy, disappearance of glandular tissue and round cell infiltration. The pathogenesis is not clear. It is probable that the cerebral changes occurred as the result of intestinal autointoxication, faulty detoxification due to hepatic insufficiency, hypovitaminosis and perhaps hypochloremia due to vomiting. Neubürger suggests that chronic gastritis may be the important factor in accounting for the frequency of Wernicke's disease in cases of alcoholism.

SAVITSKY, New York.

CIRCUMSCRIBED ATROPHY OF THE BASAL GANGLIA. FRANCESCO BONFIGLIO, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:306 (Nov.) 1937.

Bonfiglio reports a case of recurring manic-like episodes in a man aged 35 without a history of previous mental disease. The attacks occurred frequently, with periods of relative freedom lasting a few weeks, and were characterized by grandiosity, overactivity and euphoria. Neurologic and serologic examinations gave normal results. During this period there was definite tachyphemia (festination of speech). This first phase of the illness lasted four years. The excitement and euphoria gradually became less marked, and intellectual enfeeblement appeared, at first for complex and then for simpler psychic functions. During the early part of the second four year period poor judgment, inadequate and inappropriate affective responses and lack of interest were noted. Orientation, memory and simple calculations were intact. The relative sparing of the elementary psychic functions continued for two years. Festination of speech was soon followed by palilalia. During spontaneous speech and in response to questions, the last few words, or even a whole sentence, was repeated, at first from two to four times and later as many as twenty times. Later still, even parts of words were repeated many times (logoclonus). These speech disturbances appeared during the fifth year of the illness and continued to the end except for a period of mutism of seven months with onset one year after the speech disorder became manifest. Palimimia was present throughout the illness. There was no palingraphia. Dysarthria, aphasia and echolalia were not noted. There was no parkinsonism or other extrapyramidal phenomena. During the last few months there was marked marasmus.

Autopsy showed generalized atrophy of the cerebral hemispheres with more pronounced atrophy of the basal ganglia, especially the cephalic part of the caudate nucleus. Microscopic examination showed diffuse parenchymatous degenerative changes in the whole brain, especially the head of the caudate nucleus and the oral parts of the putamen and pallidum. The large nerve cells of the caudate nucleus, putamen and pallidum were particularly involved. There were no senile plaques. There was mild gliosis throughout the affected parts of the brain. Bonfiglio believes that this parenchymatous degeneration is a variant of Pick's disease. There have been 4 other cases of Pick's disease with similar distur-

bances in speech. The author's case differs from those previously recorded in the fact that there was no associated extrapyramidal involvement and no evidence of aphasia.

SAVITSKY, New York.

TUMORS OF THE BRAIN. O. GAGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:69 (March) 1938.

Gagel found that 4.6 per cent (560) of all patients admitted to an active neurologic service had tumors of the brain. In 198 of these cases the tumors were in the cerebral hemispheres; in 150, at the base of the brain; in 118, in the spinal cord, and in 56, in the cerebellum. In addition, there were 34 cases of tumors of the cerebellopontile angle and 2 of tumors of the peripheral nerves. The large number of tumors at the base of the brain is noteworthy; 54 of these were in the chiasmal region, 19 in the basal ganglia, 9 in the thalamus, 15 in the third ventricle, 22 in the region of the corpora quadrigemina, 17 in the fourth ventricle and 14 in the pons and medulla. Three hundred and five of the tumors were of neuroepithelial origin. In the other group of 255 tumors there were 76 meningiomas, 7 neurofibromas, 31 metastatic tumors, 29 sarcomas and carcinomas, 22 hypophysial adenomas, 17 craniopharyngiomas, 10 hemangioblastomas, 7 hemangiomas, 10 cysticercus cysts, 8 chondromas, 6 epidermoids, 2 dermoid cysts, 6 lipomas, 6 arachnoid sarcomas, 6 cysts, 4 tuberculomas, 2 teratomas, 2 osteomas, 2 gummas, 1 chordoma and 1 melanoma.

Gagel limited his study to tumors of neuroepithelial origin. There were 2 neuroepitheliomas, both arising from the floor of the third ventricle. There were 25 medulloblastomas (13 in males and 12 females); 19 were in the vermis and 2 in the cord; there were 1 each in the third ventricle, pons and temporal lobe and 1 in the retina and optic nerve. There were 9 cases of gangliocytoma, tumors composed predominantly of ganglion cells. These tumors all occurred in young persons, 6 in males and 3 in females, especially in the brain stem.

In 16 cases the tumor was a polar spongioblastoma (9 in females and 7 in males). Most of these occurred in the later half of life. In most instances the tumor was located in the brain stem and was inoperable. There were 4 cases of astroblastoma in the white matter of the cerebral hemispheres and in the corpus callosum. The characteristic attachment of the main process to the blood vessels was readily seen. There was little fiber formation. Astrocytomas were more numerous (58 occurring in 32 males and 26 females). Most of these tumors were observed in young persons, owing to the high incidence of cerebellar astrocytomas. Twelve were in the cerebellum; 22 in the cerebral hemispheres; 5 in the third ventricle; 4 each in the fourth ventricle, pons and cord; 3 in the basal ganglia, and 2 each in the thalamus and corpus callosum. Most of the hemispheral tumors were in the frontal lobe.

Glioblastoma multiforme, or malignant glioblastoma, is the commonest gliogenous tumor. There were 84 cases of such tumors in the series (55 of which occurred in men and 29 in women). These tumors were seen especially in the cerebral hemispheres. None were observed in the cerebellum. They were encountered most frequently about the fortieth year. Three types of such tumors can be clearly differentiated: the microcellular glioblastoma, containing the small cells resembling medulloblasts; the fusiform glioblastoma, with long cells resembling polar spongioblasts, and the glioblastoma multiforme, containing polynuclear giant cells and characterized by intense polymorphism. Mitoses were most numerous in the small cell glioblastoma. This microcellular glioblastoma may extend into the leptomeningeal tissues.

There were 5 oligodendrogliomas—3 in the cerebral hemisphere and 2 in the spinal cord. They were slow-growing tumors and usually contained relatively large deposits of calcium. They were subcortical and not sharply delimited from the normal brain tissue. Thirty cases of ependymoma (21 in men and 9 in women) were observed. The ages of the patients ranged from 20 to 40. The most common site was the region of the fourth ventricle (7 cases) and the spinal cord

(7 cases). In 5 cases each the region of the third ventricle and the aqueduct were involved; in 4 cases the lateral ventricle was the site, and in 1 case each the cerebellum and the cortex were implicated. Six cases of papilloma of the choroid plexus were seen—in 4 cases the tumor was in the fourth ventricle, in 1 in the foramens of Monro and in 1 in the occipital lobe. Calcification and implants from the spinal fluid were seen. There were 11 cases of pinealoma, with the usual predominance (9 cases) in males.

SAVITSKY, New York.

CEREBROVASCULAR CHANGES ASSOCIATED WITH TUMOR OF THE BRAIN. G. BODECHTEL and G. DÖRING, Ztschr. f. d. geş. Neurol. u. Psychiat. **161**:166 (March) 1938.

Bodechtel and Döring studied circulatory changes far removed from the site of the tumor in cases in which operation was performed and in those in which there was no operation They observed microscopic hemorrhages at a distance from the tumor; these hemorrhages could not be considered agonal because they were usually too extensive. Cell changes in the neighborhood pointed to a process of longer duration. It is unlikely that the lesions were Duret's hemorrhages, which are usually seen in cases of trauma. Necrotic changes in tissue about the hemorrhages were also seen. Both the ganglion cells and the glia elements were involved. Perivascular edema was noted in some cases. The hemorrhages varied in size from small perivascular hemorrhages to massive extravasations and were observed both after operation and when no operation had been performed. In most cases there was considerable associated cerebral edema. The hemorrhages must be considered as the probable cause of death in some cases of tumor. Necrotic areas were not infrequently noted, especially in cases of spongioblastoma multiforme. Areas of ischemic necrosis were seen most frequently in the cornu ammonis and the inferior olives. Such changes have been seen in very young patients. These anatomic changes explain the occasional fleeting palsies which cannot be accounted for except by a lesion at a distance from the tumor. It also throws light on the nature of occasional postoperative complications, such as psychotic states.

SAVITSKY, New York.

HISTOLOGIC CHANGES IN THE NERVOUS SYSTEM IN EXPERIMENTAL COMPRESSION OF THE SPINAL CORD. K. ITO, Psychiat. et neurol. japon. **42**:31 (May) 1938.

Ito studied the effect of relatively slow experimental compression of the spinal cord in two groups of rabbits: (1) a group in which the cord was compressed and the animals were killed and (2) a group in which the cord was compressed for from three to ten days, with removal of the compression after this period. There was at first flaccid, and later spastic, paralysis in the hindlegs, accompanied by increased reflexes, temporary disturbance in bladder control, loss of weight and increase in albumin, but no pleocytosis. The paralysis disappeared in cases of temporary compression. The significant histologic changes were in the compressed segment and its vicinity. They consisted of hyperemia of the vessels in the spinal cord and pia, acute swelling of the ganglion cells and swelling of the axis-cylinders. From these observations, Ito concludes that the compression paralysis was produced by destruction of the nerve elements, which might be elicited in part by the toxic effect of destruction of the blood cells, which in turn was closely related to the stasis of the blood and lymph in the spinal cord.

ALPERS, Philadelphia.

## Psychiatry and Psychopathology

THE ABNORMAL AMONG THE OJIBWA INDIANS. RUTH LANDES, J. Abnorm. & Social Psychol. **33**:14 (Jan.) 1938.

The essential contribution which the anthropologist can make to the study of the psychoneuroses is in articulating his descriptions of psychic disorders with the

conflicts and modes of life of the peoples among whom they are found. All societies are not equally provocative of psychoneuroses, and in many cultural milieux grave disorders do not flourish to the same extent as among the Ojibwa Indians or the white race. The peculiar personality traits of the Ojibwa are not direct reflections of environmental pressures but cultural developments which are absent in other similarly situated tribes. The Eskimos know nothing of the obsessive anxiety of the Ojibwa, although their Arctic resources are slim enough and recurrent famine is a commonplace among them. Famine actually strengthens the bonds of an Eskimo community. If cannibalism occurs, it is in order that the most capable adult be given strength to hunt for the group.

The ethos of the Ojibwa is saturated with anxiety, which has a realistic basis in the oft recurring periods of starvation. Ojibwa culture does not provide a traditional hierarchy in which a man can find his place and, in so doing, find a measure of security. Rather than rely on weak and competing human beings around him, the boy is told to seek a patron and companion among supernatural beings, to whom he turns for comfort and aid and whom he visualizes often in the shape of the great animals he desires to kill. The man who gains prestige is one who exerts power over people for his own private ends. When he is successful, he is regarded not as having attained security but as having become more vulnerable to *windigo*—the neurotic and psychotic manifestation of his severe anxiety with reference to food, expressed in terms of melancholia, violence and obsessive cannibalism. The Ojibwa says that he is possessed of the *windigo* spirit sent on him by a sorcerer and that he must serve the appetites of the *windigo* as his own. *Windigo* is the mythologic and supernatural figure, a giant skeleton made of ice, that flourishes in the wintertime only and is an insatiable cannibal. It epitomizes all the unhappy souls who die of starvation in the winter; it is a frenzied character who howls and crashes through the land, threatening swift and horrible doom.

*Windigo* insanity among shamans (sorcerers) means conflict to the death. Ordinarily, women do not succumb to *windigo,* since they are not activated by drives to power and, even while they may temporarily use masculine technics to meet specific emergencies, their objective is the satisfaction of a need rather than a drive to power. However, the women who have from earliest childhood been reared to assume a masculine role may fall into *windigo* or suffer other disintegrations of personality. The things which make a capable man a more conspicuous target for envy—the culturally inculcated masculine pursuit of power, the ideas of personal reference, the penalizing of success—are the aspects of Ojibwa male ethos underlying the marked neuroses and psychoses which are termed *windigo.*

WISE, Howard, R. I.

JUDGING PERSONALITY FROM EXPRESSIVE BEHAVIOR. STANLEY GODDARD ESTES, J. Abnorm. & Social Psychol. **33**:217 (April) 1938.

Estes attempted to find out whether personality traits can be ascertained from moving pictures taken while the persons under study performed simple everyday actions, such as removing a coat and shirt, playing a game or attempting to push another subject off balance. The true personality characteristics of the actors were known to the experimenters, but not to others. It was shown clearly that some persons who were photographed could be judged more accurately by their expressive behavior than could others. It was found that those who possessed a preponderance of introvertive character traits could be least accurately judged; particular aspects of personality, such as those related to inhibition, emotional intensity and self assertiveness (or their opposites), were conspicuously easy to judge. Finally, it was concluded that general judgment of the personality in its entirety is more accurate than judgments based on minute analysis of each characteristic.

WISE, Howard, R. I.

FACE-HAND LATERALITY IN RELATION TO PERSONALITY. JOHN G. LYNN and DORIS R. LYNN, J. Abnorm. & Social Psychol. **33**:291 (July) 1938.

The authors attempted to find a relationship between the dominance of the muscles of one side of the face and right or left handedness and to determine the relation of these to personality. Only persons who were unanimously judged to have excessive motility of one or the other corner of the mouth were selected for the tests. If the right hand and the right side of the face were dominant the term "homolateral hand-face dominance" was used. However, if the right-handed person favored the left side of the face while smiling the term "contralateral hand-face dominance" was employed. There were the crossed and the uncrossed type of hand-face laterality. It became obvious that there were two definite and opposite types of personality, which recurred regularly and were associated with the two opposite kinds of hand-face relationship. These contrasting personality types were labeled "P," positive, and "N," negative, and were expressed in terms of fifteen parallel contrasting tendencies, such as "aggressive-retiring"; "leader-follower"; "dominating-subservient," and "secure-insecure" (socially). Through statistical methods, a correlation of 77.5 per cent was found between the hand-face relationship (crossed and uncrossed) and the general trend of personality.

It was concluded, therefore, that the functional relation between hand dominance and clearcut lateral dominance of involuntary facial expression serves as an indicator of a fundamental dichotomy of personality. It was postulated that, other factors being equal, homolateral hand-face dominance is a reflection of a better integrated, more direct unilateral neural action pattern, chiefly mediating the positive reaction tendencies. Conversely, there is a negative reaction tendency to be found in the contralateral hand-face subjects.

WISE, Howard, R. I.

THE PSYCHOLOGICAL EFFECT OF BENZEDRINE SULPHATE. PAUL SCHILDER, J. Nerv. & Ment. Dis. **87**:584 (May) 1938.

Schilder observed the effect of benzedrine sulfate on 2 patients who were undergoing psychoanalysis. In both cases benzedrine gave satisfaction at an incompletely genitalized level, reduced the sexual tensions, increased narcissistic pleasure in the body and its own energies and hence enabled the patient to feel himself loved by himself and others. There were a subjective sense of tension and restlessness, definite insomnia and a negative after-reaction which dissuaded one patient from the continued use of benzedrine. Schilder thinks the results depend on the structure of the personality as well on the drug and suggests that benzedrine may help to reveal material important to the analysis.

MACKAY, Chicago.

ADAPTATION TO REALITY IN EARLY INFANCY. THERESE BENEDEK, Psychoanalyt. Quart. **7**:200, 1938.

Benedek points out that infants who have been raised in a hospital, who suffered from lack of love or too rigid a routine, differ in their adaptation to reality from infants whose routine has been adapted to their physiologic needs and whose mothers have loved them. In the second group, the infant's ego is assured, enhanced by a reliable ally, the mother, who regulates the things of the outer world and saves the child from anxiety. The ego, strengthened, on the one hand, by the libidinal relation to the mother and, on the other, by the absence of anxiety, has a greater capacity to perceive the objects of the outer world. This ego is able to accept new and unexpected situations and to master them by trust in the mother. In the adaptation to reality it has a greater span and a greater versatility. In the first group, the infant is deprived of its powerful ally, the mother, to whom the child capable of waiting can turn with the conviction that help and satisfaction will come from her. The infant who cannot entrust itself to the mother is left alone; it turns its attention libidinally not to the mother but to the objects surrounding it. It is abandoned by the mother as much as by the other objects of the world and therefore concentrates its weak ego on material

things and tries to control them in an attempt to save itself from any new situation which is frightening. The infant becomes dependent on the sequence of the procedure of nursing, on the manipulations of the nursing persons and on the articles used. It cannot establish confidence as the primary object relationship, and a greater amount of anxiety develops. This anxiety has several sources. One is the body itself, which causes the infant pain by traumatic sensations of unsatisfied instinctual needs. Another source of anxiety is the real danger in which the weak ego finds itself in the object world. A third source, at a later age, is the instinctual tension which develops as a result of the disturbance of the object relationship to the mother.

Observation of children and the analysis of adults in recent years show an increasing number of rejected children and adults with the psychologic reactions of the rejected child. Benedek points out that this must result from the rigid routine laid down by pediatricians. Infants born in this hygienic age are raised by a strict ritual, which is dictated from the first moment of life by what seems to be the most important element in civilization, time. The child has to be adapted to the time regulations of the hospital or of the home. The technic of feeding as it is practiced directly contradicts all the leading principles of education. The endeavor in education is to find a way to satisfy the needs of the child which guarantees the best development of the personality; all modern studies of education are aimed toward finding methods to save the child from feelings of inferiority and from the undermining of its ego.

Why is it that in this "century of children" mothers so readily accept the rigid type of hygiene as the highest precept in their relationship to their infants? Why do they relinquish so easily their emotional relation to the child and often "reject" it with the rationalization that they are doing only what is permitted and, therefore, what is best? It is probable that mothers tend at present to make their children adhere to schedules for the sake of the schedule, not for the sake of the child, for this is "the century of the woman." It is the emancipation of women that elevated nursery hygiene to its present height and, with the help of narcissistic satisfaction, intellectualized the mother's relationship to the child.

PEARSON, Philadelphia.

A PSYCHOANALYTIC STUDY OF A CASE OF CHRONIC EXUDATIVE DERMATITIS. LEO H. BARTEMEIER, Psychoanalyt. Quart. **7**:216, 1938.

Bartemeier describes the successful analysis of a dentist with chronic exudative dermatitis of the hands. The lesion on the hands represented a punishment for hostility to men in authority (his father). It protected him from the danger of being castrated and served as a restitution for his own desires to castrate the father. At the same time, by causing him suffering and inconvenience, it permitted him to gratify a partial impulse of voyeurism, exhibitionism, sadism and masochism and a desire to steal. It also provided masturbatory gratification. It disappeared after he was forced to adhere to the financial arrangements with the analyst which he had originally agreed to and which he was avoiding by a number of excuses. Thus, threatened by the firm father who demanded payment, he began to make restitution. His castration anxiety was stimulated, and the lesion no longer protected him from dread. He was forced to give up the partial gratifications and to make restitution in order to avoid castration anxiety and to receive love from the analyst in the role of the father.

PEARSON, Philadelphia.

THE USE OF HOSTILITY AS DEFENSE. LEWIS B. HILL, Psychoanalyt. Quart. **7**:254, 1938.

Hill points out that negative reactions may be of two types: (1) the abreaction of a childhood anger in response to a real frustration in childhood, and (2) the use of hostility to protect the patient from becoming involved in a situation similar to one in childhood in which he experienced a real frustration. The second type,

i. e., the use of hostility as a defense against more sincere affective reactions to the analytic situation, is found in patients who were intelligent children brought up in an emotionally destructive household where they received no affectionate support from the mother. They have experienced acutely a need for love, for dependence on a mother's affectionate care, and this need has been bitterly frustrated. They have had abundant reasons for feeling hostility in childhood, but they became docile children, had delayed adolescence and learned to exploit hostility as a defense against the pain of repetition of rejection and insult in a passive relationship with a mother.

PEARSON, Philadelphia.

THE WORLD OF THE COMPULSIVE PATIENT. V. E. VON GEBSATTEL, Monatschr. f. Psychiat. u. Neurol. **99**:10 (April) 1938.

Using 3 cases as illustrative material, von Gebsattel attempts to show that compulsive disorders are associated with a special type of existence, the patient living in a world which differs in a specific manner from that of the normal person. Compulsive acts represent a defense from thoughts of death, disguised or obvious. The world of the compulsive patient is a world of hostile forces from which phenomena that appear harmless and natural to normal persons are completely excluded. The primary disturbance consists in inhibition of self development, which is experienced as a threat to the integrity of the personality. As a result, the patient notices only disturbing and destructive forces, such as death and uncleanliness, and he reacts by systematically attempting to avoid all objects and thoughts which represent, directly or symbolically, these destructive tendencies.

ROTHSCHILD, Foxborough, Mass.

PERIODICITY IN MANIC-DEPRESSIVE PSYCHOSIS. ELIOT SLATER, Ztschr. f. d. ges. Neurol. u. Psychiat. **162**:794 (June) 1938.

One hundred and sixteen cases of manic-depressive psychosis were studied statistically. Most of the cases occurred during the early summer, with another, less marked, increase during the early spring. There was a tendency in each patient for the attacks to recur during the same season and for the intervals between the attacks to be similar. Each patient had his own rhythm. There was no cogent evidence that the interval between attacks became shorter or that the attacks lasted longer as the patient grew older. It should be borne in mind that older manic-depressive patients are more readily hospitalized and usually are not discharged as soon as younger patients.

SAVITSKY, New York.

## Meninges and Blood Vessels

PNEUMOCOCCUS MENINGITIS WITH RECOVERY. WARDE B. ALLAN, SIDNEY MAYER and RUSSELL WILLIAMS, Am. J. M. Sc. **196**:99 (July) 1938.

The authors report 3 cases of pneumococcic meningitis successfully treated with sulfanilamide. The organisms concerned were types XXIV, XXIX and XX. The sulfanilamide was given orally in all cases and intrathecally and subcutaneously as well in the third case.

MICHAELS, Boston.

MENINGO-ENCEPHALITIS IN MUMPS. H. FINKELSTEIN, J. A. M. A. **111**:17 (July 2) 1938.

Finkelstein performed spinal punctures as a routine on practically all patients with mumps admitted to the Willard Parker Hospital. In about 40 patients spinal puncture was performed as soon after admission as was feasible. Complete physical and neurologic examinations preceded the spinal puncture. Sixteen cases in which the spinal fluid was abnormal are reported. They were divided into

three groups: group A, in which the condition was severe; group B, in which it was mild, and group C, in which the patients were free from symptoms. The 4 patients in group A, at some time during the first week of their illness, had severe clinical signs and symptoms of involvement of the central nervous system. These patients presented extreme drowsiness, severe headache, malaise, fever and vomiting. They sometimes presented abnormal neurologic signs. The symptoms persisted for several days, the lethargy lasting from three days to a week. Headache persisted for from four to five days. Sedatives were resorted to, since spinal puncture did not relieve the patient from the headache. The 6 patients in group B had mild symptoms, including slight headache, listlessness, anorexia and slight fever. These symptoms were so mild and of such short duration that under ordinary circumstances one would not consider the diagnosis of meningoencephalitis or resort to lumbar puncture for diagnosis. The symptoms did not last for more than a few hours and were not severe enough to require sedation. The 6 patients in group C did not present any sign or symptom clinically which suggested the possibility of meningoencephalitis. They were all free from symptoms, although in some cases there occurred a slight rise in temperature for from twelve to twenty-four hours. Examination of the spinal fluid in all 16 cases showed an increase in the cell count. The fluids with the higher cell counts were hazy. The counts did not vary with the severity of the disease, since high counts were found in some cases of the mild form. All smears showed an increase in cells with great preponderance of mononuclear cells. The proteins of the spinal fluid were increased quantitatively in all cases.

EDITOR'S ABSTRACT.

ARACHNOIDITIS LIMITED TO THE FOURTH VENTRICLE. DUCUING, RISER, BECQ and GÉRAUD, Rev. d'oto-neuro-opht. **16**:180 (March) 1938.

The authors report the case of a woman aged 36 who had had severe occipital headaches for four months, sometimes accompanied by cerebral vomiting. Complete examination revealed nothing abnormal except symmetric distention of the lateral ventricles, bilateral papillary stasis and recent hemorrhages in the right fundus oculi. Suboccipital decompression revealed arachnoiditis, limited to the fourth ventricle. The roof of the ventricle was thickened, and the foramens of Luschka and Magendie were completely obliterated. The roof of the fourth ventricle was removed, and six courses of roentgen therapy were given. Examination made four months later revealed complete absence of symptoms and disappearance of the papilledema.

DENNIS, San Diego, Calif.

BEHAVIOR OF BLOOD PRESSURE DURING OPERATIONS FOR TUMOR OF THE BRAIN. W. MORITZ, Deutsche Ztschr. f. Nervenh. **146**:232, 1938.

Moritz observed a marked fall in blood pressure during the course of 46 per cent of operations on supratentorial tumors. Often the pulse rate fell also, suggesting irritation of the vagus nerve. This circumstance occurred especially in cases of glioblastoma and meningioma and was always accompanied by edema of the brain. An increase in blood pressure was observed in 52 per cent of cases of infratentorial tumor. In 2 cases in which a decrease of pressure occurred the tumor was a meningioma. Both types of alteration in blood pressure are to be taken as danger signals.

PUTNAM, Boston.

## Diseases of the Brain

EPILEPTIC REACTIONS: AN ATTEMPT AT CLASSIFICATION. ARTHUR GUIRDHAM, J. Ment. Sc. **83**:679 (Nov.) 1937.

Guirdham describes four clinical types of epilepsy. The first is progressive epileptic deterioration, which corresponds roughly to what in the United States is usually described as epileptic personality. In this type the author stresses

extreme egocentricity, egoism and marked explosiveness of temperament. Between the dramatic outbursts the epileptic person betrays a severe degree of emotional apathy. In the second group the author places epileptic retardation, in which some degree of mental defect is present from an early age. This group includes both congenital forms and those in which epilepsy develops at an early age. In many cases of this type there are associated gross lesions of the cerebrum and central nervous system and various stigmas and abiotrophic peculiarities which explain convulsive phenomena. The third group consists of essential epilepsy. The convulsive element is the most striking feature in these cases; psychologic degeneration is not marked. Most of the cases of epilepsy in which the patient is ambulatory fall in this group. In the fourth group are included the "epileptic abreactions." This is a type of epilepsy chiefly precipitated by psychologic factors, with a far greater proportion of psychologic manifestations than in the previous groups. This new category includes conditions previously called "hysteria with epileptiform convulsions," "hysteroepilepsy" and "psychogenic epilepsy."

In discussing the relationship of epilepsy to hysteria, Guirdham stresses the similarities between epilepsy and hysteria. He looks on epilepsy as an expression of two forces, the instinct of self-preservation and that of self-assertion, both of which find expression in the convulsive syndrome.

KASANIN, Chicago.

THE CLINICAL FEATURES OF CENTRAL PAIN. GEORGE RIDDOCH, Lancet **1**:1150 (May 21); 1205 (May 28) 1938.

Both Dusser de Barenne and Foerster showed that stimulation of the posterior horns and sensory tracts of the spinal cord is capable of producing, in the first instance, ipsilateral pain and hyperalgesia in the corresponding segments and, in the second, contralateral pain. Syringomyelia is an important chronic condition which produces central pain. In cases of extramedullary neoplasms local pain at the level of the lesion is one of the earliest symptoms, whereas the discomfort caused by intramedullary masses usually is diffuse, spreading through several segments. Aberrant sensations are present in cases of disseminated sclerosis and subacute combined degeneration, but these are "rarely painful."

A critique of the views of Head and Holmes (1912), Foerster and Penfield and Boldrey tends to show that in cases of cortical and subcortical lesions the optic thalamus is the chief organ for the reception of pain and that the cortex has a discriminatory function. Suprathalamic lesions, such as cerebral softenings, may give persistent pain and hyperpathia, resembling typical thalamic syndromes. According to Head, pain consists of two elements: a true specific sensation and an unpleasant feeling tone. It is necessary to differentiate between "spontaneous" and "evoked" pain. The emotional state of the patient, as well as the type of peripheral excitation, is important in the "receptivity to pain." The function of the autonomic nervous system in the pathogenicity of central pain is ambiguous, except for sensory impulses from the viscera. The sensory gray matter is much more important in the pain receptive mechanism than is the white matter. On the basis of the work of Sherrington, Head and Thompson and others, the conclusion has been reached that inhibition is the physiologic means by which pain is controlled through neural mechanisms. It is only when massive stimulation occurs that pain may be perceived. Then, not only the spinothalamic tracts but tracts in the posterior column or short reflex relay arcs may come into play. Both stimulation and inhibition are important variables in the pain-receiving mechanism. These are finely integrated with individual vulnerability along neurophysiologic lines.

KRINSKY, Boston.

A CASE OF ISOLATED SENSORY AMUSIA AND PARTIAL SOUND AGNOSIA. OTTO KAUDERS, Jahrb. f. Psychiat. u. Neurol. **54**:119, 1937.

Kauders reports a case in which there was an isolated acoustic-gnostic disturbance without aphasia, apraxia or other evidence of damage to the brain and with excellent preservation of intelligence. The case demonstrates that distur-

bances in the sound and understanding of words are independent of disturbances in understanding of other acoustic impressions, especially of musical sounds. The case is also an exquisite example of genuine sensory amusia, with almost complete loss of understanding and recognition of isolated tone formations, tone succession, accord and melodies and corresponding inability to produce images of this kind. The almost complete loss of the impressive components of musical perception gave rise to absence of expressive imagination of tone formation. The patient was not more than an average lover of music, his entire musical activity consisting of singing in a chorus. In spite of the absence of special musical inclinations in this case, the question arises whether the musical disturbance is to be regarded as genuine sensory amusia or a gnostic disturbance. In this connection, Fruchtwanger's differentiation of actual gnostic disturbances, amusias and central anakusias assumes considerable significance. According to this author, when a patient complains that he hears all sounds as louder and shriller than normal he can hardly be regarded as having a gnostic disturbance, for in such disturbances one is dealing with a disturbance not in the sphere of acoustic imagery but in the central auditory apparatus, i. e., central paracusia. Whether this hearing of overtones is of the same nature as that observed in diseases of the peripheral acoustic apparatus or of the middle ear cannot be definitely determined.

The patient was unable to follow a tune correctly or to follow and count correctly several successive acoustic signals such as song tunes, piano tunes, flute sounds and tap signals. In attempting to follow a tune, the patient invariably went "off key" and not only attempted to follow in the same key but was compelled to employ a sort of paraphasia, in the course of which he added several more tunes. This, Kauders believes, was due not solely to a musical disturbance but to defective perception and elaboration of acoustic impressions, for this paraphasia-like phenomenon was also observed during hearing, estimation and following of tap signals. Not only was the rhythm incorrect when the patient attempted to follow tap signals but there was also difficulty in counting the signals. This, however, was not merely a defect in the sense of rhythm, which was unquestionably also affected, but a marked disturbance in the motor-expressive sphere. It is noteworthy that the patient insisted repeatedly that he did not hear individual tones and noises but that there was a "running together" of them, so that he heard a "little melody." Apparently, both melody and rhythm were equally affected.

In spite of the severe disturbance in the patient's appreciation of music, his ability to recognize to a certain extent the total character of his favorite musical scores was well preserved. According to Kauders, in many cases of disturbance of musical appreciation, the musical experience is so closely associated with the patient's mental life, especially with his emotions, that it transcends the disturbance in acoustic perception and in the musical sphere. This transcendental and preeminently emotionally toned musical experience is only loosely connected with the gnostic sphere of musical appreciation and may not be entirely lost, even though the latter is severely affected.

Although there is little definite knowledge of the relationship between amusia and disturbances of sensory impressions for nonmusical sounds, the case reported seems to indicate that it is probably close. It must also be borne in mind that amusia may be present when recognition of sounds is intact, whereas, on the other hand, sound agnosia may occur without demonstrable evidences of disturbance in the appreciation of music.

KESCHNER, New York.

RELATIONSHIP OF MENTAL DISTURBANCES AND DISORDERS IN SPEECH ASSOCIATED WITH DEMENTIA PARALYTICA: SYNDROME OF DYSARTHRIA, PALILALIA, AGRAMMATISM AND FACIAL APRAXIA. ERWIN STENGEL, Jahrb. f. Psychiat. u. Neurol. **54**:150, 1937.

Stengel describes in detail a case of Lissauer's dementia paralytica in which there were severe dysarthria, palilalia, agrammatism in the sense of a telegraphic

and Negro style and facial apraxia. He observed a similar syndrome in 3 other cases of focal dementia paralytica. In his opinion, this syndrome represents a severe type of speech disturbance associated with this disease, which may be observed also in the terminal stage of nonfocal dementia paralytica. The organic substratum of this speech disorder is a severe pathologic process in the anterior portion of the striatum, as well as the foot of the third frontal convolution and the areas adjoining. Stengel stresses the importance of recognizing that the basis for the telegraphic style in this disorder is not aphasia. He regards the telegraphic style as evidence of poverty of speech, which is associated with motor, and especially with apractic, difficulties in the speech act, as well as with unusual rapidity of speech leading to speech pulsion and, finally, to palilalia. Agrammatism is also regarded as being due to poverty of speech.

KESCHNER, New York.

CHOLESTEROL METABOLISM ASSOCIATED WITH MULTIPLE SCLEROSIS. CHARLOTTE FRISCH, Wien. klin. Wchnschr. **50**:596 (May 7) 1937.

After pointing out that some authors regard multiple sclerosis as an infectious disease in which the causal agent is in the central nervous system, Frisch suggests that the disorder in the central nervous system may be the manifestation of fermentative processes and their defense reactions. This would not impair the theory of an infectious origin; in fact, it suggests the possibility that the causal agent is in a region other than the central nervous system. The substances which have a lytic effect particularly on the medullary sheaths of the central nervous system should be lipases. To be sure, these would not be demonstrable in vivo, but if lipase is present in the central nervous system, cholesterol esterases capable of intercepting and binding these lipases might be formed. In this case there would be an increase in the cholesterol content of the serum of patients with multiple sclerosis. The total and the free cholesterol were determined for 12 patients with multiple sclerosis, 3 patients with amyotrophic lateral sclerosis, 1 patient with neural myatrophy and 2 patients with chronic poliomyelitis. Then, tests for cholesterol tolerance were made. For the patients with multiple sclerosis the cholesterol values were extremely high. However, the ratio of free to esterified cholesterol was normal. The suggestion that the increase in cholesterol may be due to the decomposition of the medullary sheaths is refuted by the observation that in cases of the other disorders, such as amyotrophic lateral sclerosis and chronic poliomyelitis, the cholesterol values were normal. It is further pointed out that since the cholesterol metabolism is closely related to the adrenal cortex and the adrenal glands take part in vitamin metabolism, it is possible that multiple sclerosis belongs to the group of vitamin deficiencies. On the basis of this theory, the patients with multiple sclerosis were treated with vitamin C. It was found that after four weeks of this treatment the cholesterol content had become reduced. Frisch admits that the short period of observation permits no definite conclusions, and she still leans toward the hypothesis that the increase in cholesterol is the manifestation of a defense reaction against lipolytic ferments. However, this theory requires further proof.

J. A. M. A.

TREATMENT OF NEUROLOGIC COMPLICATIONS OF PERNICIOUS ANEMIA. K. HITZENBERGER, Wien. med. Wchnschr. **87**:257 (March 6) 1937.

Hitzenberger says that if funicular myelitis exists in association with pernicious anemia the most potent preparations should be used. Whereas in cases of pernicious anemia not complicated by funicular myelitis an erythrocyte count of about 4,000,000 and a hemoglobin content of 80 per cent may be regarded as adequate, in cases of funicular myelitis these are not sufficient. In the latter, efforts should be made to bring the erythrocyte count up to 5,000,000 and the

hemoglobin content to 90 or 95 per cent; even after that the injections should be continued. Depending on the severity, 2 cc. of a potent preparation should be injected daily or every second day for a period of from four to five months. Thus, it is possible to influence even the apparently hopeless forms. There is no danger of polycythemia even if the normal values are exceeded. The substances that are effective against the nervous symptoms apparently are present in such small quantities that large amounts of liver extract must be administered. There are factors which make it probable that funicular myelitis is an avitaminosis. However, there are only a few reports on the therapeutic efficacy of vitamin B when given alone. Stomach preparations are effective against funicular myelitis and should be tried. In especially severe forms they should be given in combination with liver extract.

J. A. M. A.

TRACT ENCEPHALITIS. H. HOFF and O. PÖTZL, Wien. med. Wchnschr. **87**:563 (May 22) 1937.

Hoff and Pötzl designate as "tract encephalitis" an encephalitic process of the brain stem in the course of which there can be recognized the same route of infection, namely, the "trigeminus tract," as that which Doerr and his collaborators demonstrated in infections of the cornea of rabbits with various strains of the virus of herpes simplex. Thus, the term "tract encephalitis" has been patterned after the term "tract immunization." The authors apply the term to a group of human encephalitides which they consider worthy of special investigation. They cite a case of "tract encephalitis" in a child aged 12. Wallenberg's syndrome was present, and since herpes of the cornea had preceded, infection by way of the trigeminus tract was regarded as proved. The authors describe tests on animals with the virus. It proved possible to transmit the virus to rabbits. The experiments on rabbits demonstrated the identity of the chief characteristics of the herpes virus that was obtained from the nasal secretion in a case of "tract encephalitis" with those of the encephalitogenic herpes strains studied by Doerr. However, the virus examined proved exceptional in that the spinal cord was not infectious after encephalitis had been produced by inoculation and that the brain pulp proved noninfectious after myelitis had been induced by means of intravenous inoculation.

J. A. M. A.

SIGNIFICANCE OF THE CORTEX OF THE ORBITAL SURFACES OF THE FRONTAL LOBES. H. SPATZ, Ztschr. f. d. ges. Neurol. u. Psychiat. **158**:208 (May) 1937.

Velt, in 1888, noted changes in personality and character without impairment of memory in a man with an injury to the orbital surface of the frontal lobe. Spatz became interested in the significance of this part of the brain as a result of experiences with changes in personality in a case of olfactory meningioma. There were sexual erethism, euphoria and lack of insight without any intellectual enfeeblement. Though the patient had a positive Wassermann reaction, there was no evidence of dementia paralytica on anatomic examination of the brain. Spatz also noted mental changes in other cases of subfrontal meningioma. The number of cases, however, is too small to permit any conclusions. The suitability of Pick's disease for the study of localization is emphasized, especially since the parenchymatous degeneration is usually circumscribed. In 11 cases of Pick's disease the basilar part of the frontal lobe, especially the medial and orbital regions, were observed to be most often affected. In most of the cases the base of the frontal lobe was more involved than the convexity. The medio-orbital part of the frontal lobe showed especially marked degeneration in 9 cases. This was striking in 5 cases of early involvement. Spatz adds that the basilar part of the temporal lobe is usually involved in Pick's disease. He believes that these changes in the temporal region also play a role in accounting for the mental changes, especially the involvement of more complex mental functions. The poles

and basilar portions of the frontal and temporal lobes are most frequently implicated in cases of injury to the head. In these cases, as in those of Pick's disease, the first temporal gyrus and the region of the cornu ammonis are spared. Mental changes following injury to the head are similar in some ways to those encountered in the earlier stages of Pick's disease. There is cogent evidence that the basilar cortex is phylogenetically newer and probably concerns itself more than the convexity with regulation of the more complicated mental activities of man.

SAVITSKY, New York.

HEREDITY IN EPILEPSY: IV. STUDY OF THE CHILDREN OF EPILEPTIC PATIENTS. K. CONRAD, Ztschr. f. d. ges. Neurol. u. Psychiat. **159**:521 (Sept.) 1937.

Conrad used the material collected during a census of defective persons in Wartenburg, Bavaria. This included cases of a condition classified as "repeated epileptic attacks." A thorough study of 519 patients was made. Most of the patients suffered from epilepsy of long standing and had children. The patients were divided into three main classes: those with idiopathic epilepsy, 55.3 per cent; those with an intermediate form, 24.2 per cent, and those with symptomatic epilepsy, 14.2 per cent.

The intermediate class (134 patients) needs comment. Patients with the following types of the disease were included in this group: late onset of epilepsy, between the ages of 30 and 50, 33 patients; first attack after an explosion, 14 patients; first attack after probable and definite commotio, 26 patients; neurosyphilis, 9 patients; severe alcoholism, 9 patients; suspected tumor of the brain, 3 patients; first attack after an infectious disease, such as malaria, 2 patients; typhus, 2 patients; otitis media, 1 patient, and meningitis, 2 patients. Conditions associated with deafness, blindness, hypertension, postpartum embolism, injury to the spinal column, carbon monoxide intoxication, lead poisoning, questionable tetany, early schizophrenia and diffuse sclerosis were included.

When the children who died in early infancy were excluded, an incidence of epilepsy of 6 per cent was found among the children of epileptic parents. The incidence was higher in the idiopathic group (from 6 to 8 per cent) than in the symptomatic group (from 1 to 2 per cent). Conrad believes that these figures indicate a genetic component even in the symptomatic form. The figures indicate a frequency four times as great as the average incidence in the population (0.3 per cent).

Mental deficiency was found in 16.5 per cent of the children of patients with idiopathic epilepsy, in 6.3 per cent of children of those in the intermediate group and in 2.5 per cent of children of those in the symptomatic group. The figures for the idiopathic group are high. Conrad cites as a control the normal group studied by Juda, who found from 5 to 6 per cent of mentally defective children among the siblings' nephews and nieces of normal pupils.

Psychoses were found in 3.7 per cent of children of epileptic persons, as compared with an incidence of 1.2 per cent in the general population (excluding persons with dementia paralytica). The value for the intermediate group was 0.9 per cent. There were no psychoses in the children of persons in the symptomatic group. Abnormal personalities were found in 8.4 per cent of the children of the idiopathic group, in 3.4 per cent of the children of the intermediate group and in 0.7 per cent of the children of the symptomatic group. So-called functional disorders (stuttering, enuresis, migraine, asthma, vasomotor instability and disturbances in sleep) were noted in the children of epileptic patients, with the following frequency: in the idiopathic group, 7.5 per cent; in the intermediate group, 4 per cent, and in the symptomatic group, 4.3 per cent. Morphologic disorders (clubfoot, congenital dislocation of the hip, oxycephaly, tuberous sclerosis, eczema and kyphoscoliosis) were found in 5.9 per cent of children of the idiopathic group, in 4.9 per cent of children of the intermediate group and in 1.4 per cent of children of the symptomatic group. Children of persons with idiopathic epilepsy are more abnormal than

other children in every respect. If criminals are included, 42 per cent of the children of persons with idiopathic epilepsy have some type of physical or mental abnormality. Conrad believes that there is a constitutional factor even in symptomatic and exogenous forms. Persons who react to noxious agents with the convulsive state are predisposed in some way. There is no evidence of sex linkage in the transmission of epilepsy.

SAVITSKY, New York.

GENETIC STUDIES OF CHILDREN OF EPILEPTIC PARENTS. GERHARD FRANKE, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:381 (Nov.) 1937.

Franke reports a study of 106 institutionalized epileptic patients who had at least one child 5 years of age. There were 187 children of 71 patients with idiopathic epilepsy and 97 children of 35 patients with symptomatic epilepsy. The percentage of epilepsy for the population used as a control, including only children over 10 years of age, was 0.3. With the same method of computation, the figures were 3.4 per cent for the children of persons with idiopathic epilepsy and 2.4 per cent for the children of persons with symptomatic epilepsy. If the offspring between 5 and 20 years of age were considered only as ½ unit and those over 20 as 1 unit, the figures were 3.9 per cent for the children of persons with idiopathic epilepsy and 2.6 per cent for the children of persons with symptomatic epilepsy. If children up to 30 years of age were counted as one-half unit, the figures were 5.1 per cent and 3.1, respectively. The percentage of mental deficiency for the children in this series over 10 years of age who had epileptic parents was 12.2. The figures for the average population are from 1 to 2 per cent. It must, however, be noted that 15 of 20 mentally defective children of parents with idiopathic epilepsy had mentally defective parents; the remaining 5 defective children had parents of borderline intelligence. Four of 5 of the mentally defective children of persons with symptomatic epilepsy had defective parents.

SAVITSKY, New York.

CONDITIONS SIMULATING TUMOR OF THE BRAIN. GEORG SCHALTENBRAND, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:162 (March) 1938.

Schaltenbrand calls attention to the fact that optic neuritis may be associated with headache and may simulate a tumor of the brain. The severe impairment of vision is an important differential point. Occasionally diffuse infection of the nervous system is seen in such cases. Schaltenbrand refers to cases of optic neuritis in which cerebral and cerebellar signs were marked. In 1 such case there were extensive areas of demyelination, with intense foci of inflammatory reaction in the cerebellum, pons and optic tract. In a woman aged 23 with a clinical picture of tumor of the brain the condition was found to be a diffuse encephalomyelitis with swelling of the brain. *Turmschadel,* Buerger's disease with cerebral involvement, slow thrombosis associated with arteriosclerosis, the Laurence-Biedl-Moon syndrome, hypertension and the Stewart-Morel syndrome may all be mistaken for tumor of the brain. Pachymeningitis haemorrhagica interna, syphilis of the cerebrum, aqueductal stenosis and traumatic arachnoiditis are also mentioned.

SAVITSKY, New York.

CLINICAL STUDIES OF THE RESIDUAL SIGNS OF JAPANESE B ENCEPHALITIS IN 1935. S. UYEMATSU and others, Psychiat. et neurol. japon. **41**:23 (June) 1937.

The authors studied 218 cases of Japanese B encephalitis in order to determine the incidence of residual signs. Of the patients examined, 177 were children and 41 were adults. The majority had had encephalitis from eleven to fifteen months before. In general, children showed disturbances of motility and character, and adults complained of neurasthenic symptoms. The disease was cured in 30.7 per cent of the patients (31.7 per cent of the adults and 24.7 per

cent of the children). The Japanese B encephalitis of 1935, therefore, was particularly severe in children. No cases of parkinsonism were found. Hemiplegia and other motor paralyses were found in 7.3 per cent of the children, but they were never severe. Aphasia occurred in 3.2 per cent of the children. Dementia was present in 2.8 per cent of the children and was associated with other organic disorders, such as aphasia and hemiplegia. Epileptic attacks followed the encephalitis in 1.3 per cent. Neuroses were present in 5 adults and psychoses in 2. Changes of character were present in 71.5 per cent of the children. Miscellaneous findings, especially pupillary abnormalities, were frequent.

ALPERS, Philadelphia.

EPILEPSY AND ALIMENTARY HYPOGLYCEMIA. H. J. SCHOU, Acta psychiat. et neurol. **12**:533, 1937.

Many epileptic persons show alimentary hypoglycemia sufficient to cause convulsions. The alimentary hypoglycemia can be demonstrated in about 40 per cent of epileptic patients, provided blood sugar curves are obtained for four hours. Schou analyzed 100 nonselected cases of epilepsy in patients of both sexes who were over 15 years of age. Determinations of the blood sugar were made every fifteen minutes for the first hour and every thirty minutes for the following three hours, making ten determinations in all for each test. All curves which showed a fasting level below 60 mg. per hundred cubic centimeters, a maximum rise of less than 120 mg. or a fall to below 50 mg. after four hours, were considered abnormal. Thirty patients showed a fasting level of the blood sugar below 60 mg. per hundred cubic centimeters; 34, a maximum rise to less than 120 mg. and 43, a level below 50 mg. after four hours. Thus, 43 per cent of the epileptic patients studied showed evidence of alimentary hypoglycemia. With 23 patients the sugar tolerance test was repeated two or three times, with intervals up to one year between the tests; 15 patients who had low curves during the first test showed hypoglycemia in one or more subsequent tests. Thus, in most patients the alimentary hypoglycemia was a permanent phenomenon. The average age of the 43 patients who had normal sugar curves was 39, and the average duration of epilepsy in this group was twenty-one years. The average age of the 57 patients who had hypoglycemic curves was 33, and the average duration of the epilepsy in this group was seventeen years. Thus, alimentary hypoglycemia occurred mostly in young epileptic patients with a relatively short duration of epilepsy. In 7 epileptic patients who were able to attend to their routine work and to take the usual diet, double determinations of the blood sugar were made every hour, from 7 a. m. to 10 p. m., making sixteen double determinations in all. It was found that the patients with sugar tolerance curves denoting hypoglycemia showed low sugar curves for the day. Thus, in 1 case the blood sugar level fell below 60 mg. per hundred cubic centimeters and remained at that level for several hours. In another, throughout the day, in spite of meals and work, the blood sugar level remained constantly below 60 mg. per hundred cubic centimeters. For 29 patients with low sugar curves, the average incidence of the fits per twenty-four hours was calculated for fifteen years and plotted on the curve in terms of percentages of fits for each hour of the twenty-four hour period. The curve showed two absolute peaks, one from 6 to 8 a. m. and one from 9 to 12 p. m., and two relative peaks, one from 11 a. m. to 1 p. m. and the other from 5 to 7 p. m. The absolute peak in the evening, coinciding with the first hours of sleep, appeared to be unrelated to the hypoglycemia, but the absolute morning peak and the relative noon and late afternoon peaks might be explained by the fact that it was during these periods of the day that the alimentary hypoglycemia usually occurred. The author emphasizes the importance of occult hypoglycemia as a factor inducing convulsions in many epileptic persons and discusses the treatment of convulsions so caused. The treatment may be

surgical (partial resection of the pancreas) or medical. The latter consists of a diet rich in carbohydrates, combined with administration of from 50 to 100 mg. of ephedrine three times daily.

YAKOVLEV, Waltham, Mass.

FOUR CASES OF LEUKODYSTROPHIA CEREBRI HEREDITARIA PROGRESSIVA (MERZBACHER-PELIZAEUS' DISEASE). R. FORSBERG and R. STRØMME, Acta psychiat. et neurol. **12**:639, 1937.

The authors report clinically the cases of 1 brother and 3 sisters, aged 13, 7, 5 and 4 years, respectively, who showed progressive rigidity with contracture in flexion of the lower extremities, pes cavus, intention tremor, spontaneous nystagmus, ataxia, dysarthria and mental deterioration. In 2 of the patients there was roentgenographic evidence of osteomalacic changes in the bones of the feet. A sister aged 21 showed similar symptoms in a milder degree, and 1 male cousin of the patients' grandparents was mentally deficient and dysarthric and had difficulty in walking. The authors classify the condition presented by their 4 patients as Pelizaeus-Merzbacher disease.

YAKOVLEV, Waltham, Mass.

## Peripheral and Cranial Nerves

BERIBERI IN ALCOHOL ADDICTS. N. JOLLIFFE and R. GOODHART, J. A. M. A. **111**: 380 (July 30) 1938.

Jolliffe and Goodhart describe cases of addiction to alcohol in which there is no history or evidence of previous acute or chronic cardiovascular or renal disease but in which signs and symptoms of cardiovascular dysfunction are present. The condition described in case 1 they believe to have been analogous to the acute variety of endemic beriberi described in the Orient under the name of "shoshin." This type is said to occur most frequently in persons whose neuritic signs are so mild that they are able to work or engage in vigorous muscular activity. This activity is thought to precipitate congestive heart failure, often before the neuritis is manifest. Case 2 illustrates beriberi of the mixed type. The patient showed severe peripheral neuritis and symptoms of cardiovascular dysfunction referable to both the heart and the peripheral vessels. The authors believe that the edema was largely of peripheral vascular origin. The relative mildness of the cardiac symptoms, the normal venous pressure and the total failure to respond by improvement to digitalization favor this conclusion. The presence of marked muscular atrophy associated with loss of muscle tonus may have been an additional factor in producing and aggravating edema through the production of local venous and lymph stasis. The type of cardiovascular disturbance most frequently seen in this clinic in alcohol addicts with dietary deficiencies is illustrated by case 3. When admitted, the patient presented no signs or symptoms of cardiovascular disability except marked pitting edema of both lower extremities, of eight days' duration, and enlargement of the liver. The edema rapidly subsided when rest in bed alone was maintained and the diet was inadequate in vitamin $B_1$ and in the pellagra-preventive factor. The edema recurred when rest in bed was discontinued, only to clear completely and permanently after the institution of vitaman B therapy. The manifestations of cardiovascular disturbance had a closer relation to the peripheral neuritis than to the cutaneous lesions of pellagra. In case 4 the clinical picture of beriberi of the mixed type was similar to that in case 2. The results of postmortem examination strongly supported the authors' clinical diagnosis of circulatory failure due to beriberi. Hydropic degeneration, with separation and fragmentation of the muscle fibers of the myocardium, was not demonstrated. The patient had been treated with large amounts of vitamin $B_1$ and had shown definite signs of improvement in circulation for several days before death. Under these conditions, changes in the myocardium toward normal may have occurred. The immediate cause of death is not clear. It may be that

the general hyperemia of all the viscera, including the pancreas, with the associated increase in permeability of the capillaries and transudation of fluid through the vascular walls, was the immediate cause of the acute hemorrhagic necrosis of the pancreas observed at autopsy. If this is true, all the pathologic processes present can be included in one disease syndrome, beriberi. J. A. M. A.

"ALCOHOLIC" BERI-BERI. N. L. PRICE, Lancet **1**:831 (April 9) 1938.

It has been fairly well established that chronic alcoholism is the most frequent cause of vitamin B deficiency. Furthermore, a fortuitous relationship between this condition and "dry" beriberi is said to exist and to result in the production of cardiovascular disorders. Price reports the case of a "newspaper roundsman" aged 36, who had been on a diet mainly of white bread, tea and butter, with "fat meat" once a week and two evening meals of fried fish "without butter." Only during the summer months did he drink milk, but for several years he drank from 3 to 5 pints (0.8 to 2.3 liters) of beer daily. Breathlessness, anorexia, mid-epigastric pain and edema of the legs developed gradually over a period of several months. For two weeks before admission he had subsisted "on little else but alcohol." Examination revealed evidence of congestive heart failure, with cardiac enlargement but with normal blood pressure. Tenderness of the calf and triceps muscles was present; the tendon reflexes were at first present but later disappeared. It was found later that vibration, pain and touch sensations were impaired below the knees. By means of vitamin B therapy, rest and a high caloric diet marked improvement was noted after one week. After three months of such therapy, the neurologic status returned to normal. KRINSKY, Boston.

PERIPHERAL NEURITIS ASSOCIATED WITH PYLORIC STENOSIS AND DEFICIENCY OF VITAMIN $B_1$. L. P. E. LAURENT and H. M. SINCLAIR, Lancet **1**:1045 (May 7) 1938.

Laurent and Sinclair report the case of a baker aged 32 with peripheral neuritis resulting from a neoplasm of the stomach, which had produced pyloric stenosis. Laboratory studies yielded low values for vitamin $B_1$. The polyneuritis developed after the onset of vomiting and was cured by administration of the vitamin by injection and orally. Polyneuritis reappeared when the subcutaneous administration was stopped, only to improve when the injections were resumed. It may be that vitamin $B_1$, being unstable in an alkaline medium, is diminished because of the achlorhydria which exists in such cases, or phosphorydation may be prevented so that absorption in the intestine is impossible.

KRINSKY, Boston.

SUBACUTE POLIOENCEPHALOMYELITIS. H. ROGER, P. MASQUIN and J. VAGUE, Rev. d'oto-neuro-opht. **15**:452 (June) 1937.

In a man aged 48, after a slight general infection, accompanied by herpes of the right auricle, there appeared successively paresthesias of the face and tongue and paresis of the left seventh nerve, the soft palate, the extensor muscles of the neck and the most proximal portions of the upper extremities. At a second period bilateral ptosis, accompanied by paralysis of associated movements of the eyes (in particular, those of the levator and levogyric muscles, movements downward and to the right being better preserved), and diplopia were observed. During the second period there reappeared difficulty in deglutition and involvement of the majority of the oculomotor nerves; the motor branch of the fifth nerve; the seventh, tenth, eleventh and twelfth nerves, and the first three cervical roots. The case represents a complex bulbopontopeduncular syndrome, localized in the motor nerves and composed of two clinical types: the inferior type of Leyder and the

superior type of Wernicke. There was particular electivity for certain functions: The movements of the vocal cords were perfectly preserved. Nuclear involvement can explain the diplopia, but the almost total ophthalmoplegia appears to be due to supranuclear involvement, causing paralysis of function. Involvement of the cervical portion of the cord was indicated by paresis and atrophy of the muscles of the neck and shoulders. The paretic signs were accompanied by a myasthenic syndrome, all symptoms being aggravated by fatigue and worse at the end of the day. Sensibility was intact. At autopsy no macroscopic evidence of disease of the brain was discovered. The microscopic examination is yet to be made.

The disturbance in this case falls into the classification of polioencephalitis, due to an unknown neurotropic virus. The vesicular herpes, noted in the prodromal stage, suggests a zosterian origin, although it was not accompanied by pain.

DENNIS, San Diego, Calif.

THE NEUROLOGIC ASPECTS OF B AVITAMINOSIS. F. H. LEWY, Confinia neurol. **1**:40, 1938.

By determining the strength duration curve of nerve irritability, Lewy demonstrated numerically changes in nerve function long before the appearance of symptoms or clinical signs. He found that the characteristic clinical syndrome in a number of metabolic, toxic, infectious, blood and constitutional diseases is accompanied by changes in nerve irritability and by a characteristic chronaxiometric deviation. From therapeutic experiments Lewy concluded that B avitaminosis is instrumental in producing many, if not all, parenchymatous neuropathies. The appearance of nervous symptoms in cases of partial rather than of complete lack of vitamin B and the fact that the vitamin cannot be stored in the body in appreciable amounts may explain the frequency with which B avitaminosis is seen.

DEJONG, Ann Arbor, Mich.

NEURITIS CAUSED BY PROPHYLACTIC VACCINATION AGAINST TETANUS. K. MÉSZÁROS, Deutsche Ztschr. f. d. ges. gerichtl. Med. **30**:45 (July 6) 1938.

Mészáros says that the neuritis caused by vaccination against tetanus is comparatively rare. He describes a case in his own observation. There developed an urticaria-like exanthem eleven days after the prophylactic vaccination against tetanus and then neuralgic pains in the right arm and weakness in the deltoid, anterior serratus, latissimus dorsi and infraspinatus muscles on the right side. On the basis of the relation in time and of the typical localization in the region of the fifth and sixth cervical roots, the neuritic symptoms were regarded as sequels of the protective vaccination against tetanus, the more so since no other cause of the paralysis was demonstrable. The course may be designated as favorable, since the condition of the patient improved in nine months to such an extent that he could take up his work again; even after two years, however, there remained slight impairment. The assertion of some physicians that the damage to the nerves could not have been caused by the injection of tetanus serum, since it was made under the skin of the chest, that is, at a site distant from the impaired nerve, is refuted by the fact that tetanus serum with its antitoxin content does not exert its action at the site of injection but attacks distant nerves after resorption. This is proved also by 3 other cases cited by the author. He concludes that these rare complications offer no argument against the prophylactic use of tetanus serum. Complete cure is usually obtained in about two years.

J. A. M. A.

TOBACCO POLYNEURITIS. F. V. KEPP, Deutsche Ztschr. f. Nervenh. **146**:182, 1938.

Kepp reports the case of a patient who was employed for over two years in the packing room of a factory where an insecticide containing nicotine was made.

His work consisted in canning the liquid and soldering the cans, with resultant exposure to inhalation of the steaming fluid. During the first year he had no difficulties except occasional headache and nausea. Later he had attacks of vomiting, severe headache and profuse diarrhea with increasing frequency. These symptoms disappeared when he stayed away from work, but returned as soon as he returned. A few weeks before admission he first experienced paresthesias in the arms and legs. This was followed by anesthesia and weakness of both arms and legs, worse on the left side. He was unable to walk, had cramps in the flexor muscles and dysarthria. He did not smoke and drank little alcohol.

Neurologic examination showed irregular pupils, with sluggish reaction to light and in accommodation. Motor power was grossly diminished; there was normal tone and no atrophy. There was severe ataxia of the left arm and both legs. Sensibility for pain, touch and temperature was grossly diminished and partly abolished. The area of the left ulnar nerve and the peroneal and tibial areas were most involved. The deep reflexes were diminished. The sphincteric control of the bladder and rectum was normal. Electrical examination showed normal responses.

All the symptoms subsided with rest in bed, administration of vitamin $B_1$ and electrical treatment. After one month only slight hypesthesia remained. True tobacco polyneuritis is rare. The condition in the case presented here is atypical in that amblyopia was missing. Kepp points out that tobacco polyneuritis has not been observed in persons who overindulge in smoking or chewing tobacco, but occurs only as an industrial poisoning.

HOEFER, Boston.

## Vegetative and Endocrine Systems

LAURENCE-MOON-BIEDL SYNDROME. JUDAH MARMOR and ROBERT K. LAMBERT, Arch. Int. Med. **61**:523 (April) 1938.

The Laurence-Moon-Biedl syndrome consists, in order of frequency, of six cardinal signs: obesity, retinitis pigmentosa, mental deficiency, genital dystrophy, familial occurrence and polydactyly. Obesity is present in practically all cases in which there is no doubt of the diagnosis; retinitis pigmentosa and mental deficiency occur in over 90 per cent and polydactyly is present in about 60 per cent of cases. Other associated signs, less frequently present, are shortness of stature, syndactyly, nystagmus, deafness, atresia ani, genu valgum, pes planus, microcephaly, oxycephaly, congenital heart disease and choreiform movements. Consanguinity has been found in more than a third of the cases. There is a genuine preponderance of males over females, in the proportion of 61 : 30. Seventy-seven cases were reported up to 1932. In 25 of these the complete syndrome was present; in 10 it was considered as questionably complete; in 26 there was a partial syndrome, and in the remaining 16 the diagnosis was doubtful.

Marmor and Lambert report 2 cases of this syndrome. A detailed study of the brain in 1 case revealed only small areas of hyaline necrosis in the hypophysial stalk.

It is unnecessary to have all six cardinal signs in order to make a presumptive diagnosis of the Laurence-Moon-Biedl syndrome. Retinitis pigmentosa, obesity and genital dystrophy are sufficient for the diagnosis of a partial syndrome or an allied condition. One should hesitate to make a diagnosis of this condition in the absence of retinal degeneration. Night blindness is one of the first symptoms to attract attention to the disease. The ophthalmoscopic picture may vary from scattered areas of pigmentary degeneration along the periphery and uniform narrowing of the retinal vessels to waxy pallor of the optic nerve in the more typical cases. The etiologic basis of the syndrome is unknown, but a suggested hypothesis states that the syndrome may be dependent on two factors, one of which is dominant and autosomal and the other sex linked and recessive.

BECK, Buffalo.

LOSS OF ACIDOPHILIC GRANULES FROM THE PITUITARY OF THE GUINEA PIG UNDER EXPERIMENTAL CONDITIONS OF INCREASED METABOLISM. ISOLDE T. ZECKWER, Arch. Path. **25**:802 (June) 1938.

Zeckwer observed loss of the acidophilic granules in the pituitary glands of cats from which the pancreas and both adrenal glands had been removed and to which adrenal cortex extract, and in some instances anterior pituitary extract, were administered. It was impossible to say whether the operations or the injections or both were factors in determining the degranulation. Administration of an extract containing the thyrotropic factor of the pituitary also caused loss of acidophilic granules in the pituitary gland of guinea pigs. The loss of granules was patchy, groups of cells retaining many granules alternating with bald areas containing only a few scattered granules which stained very pale.

In two groups of experiments, the pituitary glands of guinea pigs given injections of fresh pituitary from thyroidectomized rats showed a greater loss of granules than those of guinea pigs given injections of the pituitary of normal rats, while in three groups of experiments the reverse was observed. The pituitary glands of the thyroid-fed guinea pigs showed markedly degranulated acidophilic cells.

The meaning of the loss of acidophilic cells was not clear, but the following reasoning was considered: There is abundant evidence that the acidophilic cells elaborate a factor promoting growth. It is reasonable to suppose that this factor is concerned not merely with abnormal growth, as in gigantism and acromegaly, and with abnormal dwarfing but also with normal maintenance of visceral weights, and that it may permit the regeneration which replaces normal catabolism and maintains growth equilibrium. When the pituitary is massively destroyed, as in Simmond's disease, one sees not only failure of growth but atrophy of nonendocrine viscera. Under conditions of increased catabolism and loss of tissues, as seen in the guinea pig after excessive feeding of thyroid extract or after injections of rat pituitary, which stimulate the recipient's thyroid to hypersecretion, extra demand may be placed on the pituitary gland for secretion of the substance influencing growth, in order that growth may be accelerated and equilibrium restored.

It is logical to consider the possibility that loss of acidophilic granules represents exhaustion after excessive release of the factor influencing growth which has occurred in a compensatory attempt to restore growth in an animal in which tissues were wasting with the increased catabalism resulting from excess of thyroid secretion.

It seems reasonable to suppose that the state of the acidophilic cells may vary with the intensity of the demand for the substance promoting growth. A slight need over a long period might lead to compensatory hyperplasia of acidophilic cells, whereas a sudden extreme demand, as in the present experiments, might lead to discharge of all the available secretion and disappearance of acidophilic granules.

WINKELMAN, Philadelphia.

SYNDROME CHARACTERIZED BY OSTEITIS FIBROSA DISSEMINATA, AREAS OF PIGMENTATION AND GONADAL DYSFUNCTION. F. ALBRIGHT, W. B. SCOVILLE and H. W. SULKOWITCH, Endocrinology **22**:411 (April) 1938.

The authors report 2 cases of a syndrome characterized by osteitis fibrosa disseminata and areas of cutaneous pigmentation; marked sexual and somatic precocity is found when the disease occurs in females. In a case occurring in a man aged 21 the bone age was precocious, suggesting that in the male also precocity may occur. The abdominal and cremasteric reflexes were absent, and there was decreased pain sensation on the same side as the cutaneous lesions and the majority of lesions of the bones. These findings suggest that the syndrome is due to a disseminated neurologic lesion and that the sexual precocity may be

related in some way to lesions in the wall of the third ventricle and the hypothalamus. One of the patients showed marked emotional instability, possibly also of hypothalamic origin. In only 1 case was disturbance in calcium metabolism manifested by an increased output of calcium in the urine. A number of pathologic fractures occurred, all of which healed rapidly. Biopsy of a specimen of bone taken from the skull showed characteristic osteitis fibrosa.

PALMER, Philadelphia.

CLINICAL RESULTS OF ANTERIOR PITUITARY THERAPY IN CHILDREN. M. MOLITCH and S. POLIAKOFF, Endocrinology **22**:422 (April) 1938.

Molitch and Poliakoff report the effects of glandular therapy in 32 boys who were below the minimum in height for their ages. The age distribution was from 10 to 17 years, and the standards used for comparison were Englebach's norms; determinations of bone age by roentgen examination disclosed normal values in each case. The 32 patients were divided into three groups and were treated for six months. Six boys in group A received thyroid alone; 5 boys in group B, thyroid plus anterior pituitary substance (tablets) by mouth, and 5 boys in group C, thyroid by mouth plus intramuscular injections of an extract of anterior pituitary containing the growth hormone. Eleven other boys showing similar retardation in growth served as controls. The treated groups had a larger increment in height than the controls. There seemed to be little difference in the rate of growth in the treated groups. Anterior pituitary substance when given with thyroid by mouth or by hypodermic injection produced better results than thyroid extract alone. Anterior pituitary substance given orally appeared slightly less effective than when given intramuscularly. The smallest gain in height (¼ inch [0.63 cm.]) occurred in 2 boys treated with thyroid alone and in 1 treated with thyroid and anterior pituitary substance. The largest gain in height (2½ inches [6.35 cm.]) was obtained in a boy treated with thyroid and anterior pituitary extract given hypodermically.

PALMER, Philadelphia.

## Treatment, Neurosurgery

TREATMENT OF APOPLEXY BY INFILTRATION OF THE STELLATE GANGLION WITH NOVOCAIN. W. ARTHUR MACKEY and LAURANCE D. W. SCOTT, Brit. M. J. **2**:1 (July 2) 1938.

Infiltration with procaine hydrochloride of the region of the stellate ganglion was carried out in 19 cases of apoplexy. Definite but slight clinical improvement followed the injection in 8 cases. In another case the result was considered dramatic. The patient was brought within a few minutes from deep coma to a state of clear consciousness. Mackey and Scott conclude that the effectiveness of the procedure is inversely proportional to the amount of arteriosclerosis present and to the age of the patient. The use of the method in cases of severe cerebral hemorrhage in middle-aged and older patients will serve only to bring it into disrepute.

ECHOLS, New Orleans.

TREATMENT OF MENTAL DISORDERS WITH METRAZOL. A. M. WYLLIE, Glasgow M. J. **11**:269 (June) 1938.

Wyllie used metrazol in treating 20 patients with advanced schizophrenia, 8 women and 12 men. Physical improvement was observed in 17 instances. Those who were emaciated gained from 14 to 21 pounds (6.4 to 9.6 Kg.) in weight in two months. Appetites improved, and the complexions became healthier. These 17 patients also showed increased contact with reality. One patient who had been mute for more than ten years and who had failed to react to sulfur in oil and to

sodium amytal was enabled to speak. The others became more accessible and spoke more freely. Urinary incontinence was corrected in 4 patients. Some of the patients who were previously idle were induced to occupy themselves. A patient with profound melancholia and 1 with depressive stupor recovered; 2 with chronic melancholia were much improved; 2 with resistive stupor showed slight improvement and are still receiving treatment, and 1 with obsessional neurosis improved and is still being treated.

J. A. M. A.

TREATMENT OF MENINGOCOCCAL MENINGITIS WITH SULFANILAMIDE. T. CRAWFORD and G. B. FLEMING, Lancet **1**:987 (April 30) 1938.

Crawford and Fleming treated 10 patients with meningococcic meningitis by oral, intramuscular and intrathecal administration of sulfanilamide, only 2 of the patients receiving antimeningococcus serum. Only 1 patient died, as compared with the results in a previous series of 30 patients treated with antimeningococcus serum alone, only 4 of whom recovered. Four of the patients in the present group were under 1 year of age. The authors gave from 2 to 3 Gm. of sulfanilamide daily, divided into six doses. The total dose depended on the duration of the disease and the condition of the patient. A child aged 29 months was given in twenty-six days 335 cc. of a 5 per cent solution of prontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonic acid) intramuscularly, 53 Gm. of sulfanilamide by mouth and 120 cc. of a 1 per cent concentration of sulfanilamide in physiologic solution of sodium chloride intrathecally. The patient was well in six weeks. The smallest amount given was 21 Gm. in seven days. No symptoms of toxicosis, other than cyanosis, were noted.

KRINSKY, Boston.

SURGICAL TREATMENT OF PITUITARY BASOPHILISM. A. R. D. PATTISON and W. G. A. SWAN, Lancet **1**:1265 (June 4) 1938.

Cushing's syndrome, which was originally purported to be due specifically to pituitary basophilism, has been demonstrated in cases of neoplasms of the adrenal cortex and malignant disease of the thymus. Kepler stressed the need for careful exclusion of tumor of the adrenal before the pituitary is indicted. He also recommended exploratory laparotomy as a routine, with which the authors are in sympathy. If neoplasms of the adrenal and thymus are ruled out and the presence of an adenoma of the pituitary is substantiated, high voltage roentgen therapy is advised. If this proves ineffectual, direct implantation of radon seeds into the pituitary gland is indicated. Two cases of pituitary basophilism in which this treatment was carried out are reported. In the first, that of a woman aged 26, high voltage roentgen therapy was ineffectual. Insertion of 2 radon seeds (2 millicuries each) into the pituitary gland resulted in lowering the blood pressure (to 140 systolic and 110 diastolic) and hemoglobin concentrations (to 63 per cent) and return of a normal menstrual cycle. In the second case a girl aged 16 years presented a similar picture, except that there was marked skeletal decalcification. She failed to improve after roentgen therapy and removal of part of the anterior lobe of the pituitary. Definite improvement was noted after implantation of radon seeds directly into the pituitary gland. The authors assert that implantation does not provide a cure for the syndrome. Subjective improvement is obtained, but the body configuration is changed imperceptibly.

KRINSKY, Boston.

SERUM AND SULFANILAMIDE IN ACUTE MENINGOCOCCIC MENINGITIS. H. S. BANKS, Lancet **2**:7 (July 2) 1938.

Banks reviews the results with three groups of patients with acute meningococcic meningitis: (1) 38 patients treated with serum (meningococcus antitoxin) intensively by the venous, lumbar and cisternal and occasionally the ventricular

route; (2) 59 patients treated with intravenous injection of serum and sulfanilamide by mouth, and 16 patients treated exclusively with sulfanilamide by mouth. The fatality rate in the first group during the first five days was 16 per cent. There were no infants in this series. The cerebrospinal fluid was usually sterile within from twenty-four to forty-eight hours, but in about one fifth of the cases meningococci were present for four or five days, or occasionally longer. For the 59 patients, including 10 infants treated with both serum and sulfanilamide, the fatality rate was 11.8 per cent. Recovery was rapid, and the nursing relatively easy, the cerebrospinal fluid being usually sterile within twenty-four hours. The few exceptions to this rule, as well as 2 of the 7 deaths, could be explained on the basis of low doses of sulfanilamide. Fifteen of the 16 selected patients treated with sulfanilamide alone recovered rapidly. Sulfanilamide therapy has changed the treatment of meningococcic meningitis from a difficult to a relatively simple matter. The former high mortality rate in infants appears to be yielding to this treatment. High initial doses are advocated. The sulfanilamide level in the cerebrospinal fluid preferably should reach 5 mg. per hundred cubic centimeters in twenty-four hours and be maintained at this level for three days. Early cyanosis is not an indication for reducing the dose. The treatment is probably effective only in the acute stage. Two patients treated after the tenth day of the disease died. Experimental and clinical evidence so far is in favor of combined serum and drug therapy, especially in severe forms of the disease.

J. A. M. A.

TREATMENT OF POSTENCEPHALITIC PARKINSONISM BY MEANS OF BELLADONNA ROOT. T. VON LEHOCZKY, Deutsche Ztschr. f. Nervenh. **146**:263, 1938.

The "Bulgarian treatment" was used in 64 cases, in some instances with Bulgarian and in others with local (Hungarian) roots. There seemed to be little difference between the two. The preparation recommended is a fresh decoction in white wine, made up to a standard alkaloid content of 0.6 per cent. Improvement occurred in all but 3 cases and was striking in 39. The decoction used appears to be better tolerated than atropine and to be more effective for an equal amount of alkaloid. It should be supplemented with physical therapy.

PUTNAM, Boston.

## Diagnostic Methods

SUGGESTIONS RELATING TO THE STUDY OF SOMATIC PAIN. THOMAS LEWIS, Brit. M. J. **1**:321 (Feb. 12) 1938.

Lewis states that accurate description of a pain may be diagnostic of the disease by which it is caused. This method of diagnosis will increase in value as one learns more about pain. A feature which deserves more study is the curve of pain intensity. The curve portrays the manner in which pain starts, the rapidity of its culmination, the duration and smoothness at its height and the manner of its decline. All such curves possess precise significance. It is known that a patient can accurately locate the seat of origin of somatic pain when the pathologic lesion is located in the skin or the exposed mucous membrane. However, this localization is much less accurate when deeper somatic structures, such as muscle, are concerned. The reference of pain from the diaphragm to the tip of the shoulder is an example. One of the least studied features of pain is its quality. Such terms as "tearing," "boring," "cutting," "stabbing" and "crushing" obviously have a different meaning for each person. "Burning" and "pricking" are the only terms which have universal significance. Even the terms "smarting" and "stinging" lack precise distinction, for pain of only one quality can be provoked from the skin. Under carefully controlled conditions a blindfolded person cannot tell whether he is being stimulated by a needle point, by pinching

with forceps, by pulling of a hair, by touching with a hot point, by electric current or by application of an irritant poison. All these stimuli produce a fleeting pain which is best described as a "prick." A more prolonged stimulus gives rise to pain described as "burning," but, again, the subject cannot tell whether the agent is a hot wire, a galvanic current, a steady pull on a hair or continued pinching with forceps. The difference between "pinching" and "burning" is one not of quality but purely of duration. By other experiments Lewis demonstrated that muscle pain is also of only one quality. This is most uniformly described as "aching." Likewise, web, tendon and periosteal pain are thought to be of one quality, regardless of the agent. In brief, there are only three kinds of somatic pain, namely, "skin," "muscle" and "web" pain.

Lewis suggests that in the study of somatic pain in an extremity much information may be obtained by attempting to induce an identical pain in the opposite extremity. For example, the pain of intermittent claudication may be produced in the sound limb of a patient by having him walk with a tourniquet. Another illustration is the burning of the sole with ultraviolet rays, producing a pain that is identical in quality with that of erythromelalgia.

ECHOLS, New Orleans.

MEASUREMENT OF VITAMIN $B_1$ IN HUMAN URINE AS AN INDEX OF THE NUTRITIONAL LEVEL. L. J. HARRIS, P. C. LEONG and C. C. UNGLEY, Lancet **1**: 539 (March 5) 1938.

By means of the "bradycardia" method the authors, in 1936, showed that the amount of vitamin $B_1$ in the urine can be determined and that the amount excreted after a test dose is dependent on the previous intake of this substance. Using normal subjects and surgical patients as controls, miscellaneous medical patients, patients with polyneuritis of nutritional origin, patients with polyneuritis not primarily due to disturbance in nutrition, patients with deficiency diseases other than polyneuritis and persons convalescent from beriberi, the authors found that the excretion of vitamin $B_1$ was greatest in the normal group and descreased proportionally in the others mentioned, the lowest, namely 2 instead of the normal 22 international units, being obtained in the group with polyneuritides of nutritional deficiency. Patients with beriberi yielded values of 3.5 international units or less at the resting level.

The standards for normality and deficiency were based on average values obtained under resting conditions on two or three separate days and in response to 350 international units, which was the standard test dose. An excretion of between 10 and 20 international units was considered normal for resting levels, whereas more than 30 international units was eliminated after the test dose. A resting level of less than 10 international units and an elimination of less than 15 international units after the first test dose were regarded as subnormal. Furthermore, the number of test doses necessary to bring about the normal level was an index of the state of avitaminosis.

KRINSKY, Boston.

A NEW SIGN OF HEMIPARESIS. E. HERMAN, Encéphale **1**:132, 1938.

Herman describes a new sign for the detection of hemiparesis. The nonparalyzed lower extremity is held in abduction. The paralyzed extremity is then placed in abduction and released. It undergoes a movement of adduction, often similar to the release of a spring. In brief, passive abduction of the healthy lower extremity results in adduction of the paralyzed limb. In some cases passive abduction of the healthy leg provokes adduction of the paralyzed limb without the latter being previously placed in abduction. In other cases passive abduction of the paralyzed extremity is followed by adduction of the same extremity, which returns to its initial position. The first procedure is the only one in which the

sign is elicited when it is of "low intensity." This sign has been tested in 110 cases, in 93 of which the paresis was of cerebral and in 17 of spinal origin. The sign was present in 97 cases. In most of the cases in which it was not obtained the paralysis was flaccid or in an early stage. The sign appeared when the hemiplegia began to regress or when spasticity developed. The sign was present in unconscious patients. In cases of bilateral paralysis the sign was obtained on both sides. The mechanism of the adduction sign is believed to depend on the absence of static resistance of the paralyzed extremity and the spastic contraction of the adductor muscles of the thigh. Raimiste pointed out that, normally, the adductor muscles have a higher tone than the abductor muscles. Orzechowski explained the adduction sign as follows: Passive abduction of the healthy extremity stretches the adductor muscles, which contract reflexly. This contraction serves as a stimulus for the contraction of the adductor muscles of the paretic thigh.

LIBER, New York.

# Society Transactions

## NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

MORRIS GROSSMAN, M.D., *Chairman, Presiding*

*Regular Meeting, Oct. 11, 1938*

TRANSITORY NEUROLOGIC CHANGES DURING HYPERTHERMIA. DR. RALPH T. COLLINS.

Artificial hyperthermia has been employed with increasing frequency in the treatment of various neurologic disorders. There are numerous observations on the biochemical alterations during artificial hyperthermia, but hardly any note has been made of the neurologic manifestations. Reports in the literature of post-mortem observations on patients succumbing during or shortly after hyperthermia have demonstrated that there are profound neuropathologic changes which explain the neurologic signs and symptoms appearing during the treatment. Recently, at the Neurological Institute of New York, attention was focused on the transitory neurologic changes which occurred in a patient with multiple sclerosis during electropyrexia.

A white man aged 21 received eleven treatments in the vapotherm, during each of which the temperature was elevated to 104 F. for three hours. During the sixth and seventh treatments he complained of numbness in both hands, and during the eighth, of a sensation of "pins and needles" in the hands and feet. These dysesthesias increased until, during the tenth and eleventh treatments, there developed paralysis in all four extremities. Between treatments the symptoms receded. Examination during the eleventh treatment showed: flaccid paralysis of the legs and arms; complete anesthesia to all modalities in the legs up to and including the twelfth thoracic dermatome, with the exception of the third, fourth and fifth sacral areas, over which there was partial preservation of superficial sensation; complete anesthesia to all modalities in the arms between the fifth cervical and the second thoracic dermatome; complete areflexia of the arms and legs; diminished abdominal reflexes, and a positive Babinski sign (not previously present) on the left.

The temperature was allowed to drop and within forty-five minutes reached 99 F. Neurologic examination showed partial return of motor power in all extremities, the proximal joints showing more strength than the distal. Deep sensation had returned to the pretreatment state, but there was still definite hypesthesia to superficial stimulation. Reflexes had returned almost to the pretreatment status. The Babinski sign had disappeared. That night the patient was up and felt well. On examination his status was found to have returned to the pretreatment level. For fear of producing irreversible neurologic changes, hyperthermia was discontinued, and he was discharged on May 28, 1938. When seen on August 9, he stated that he was feeling fine, that vision had improved considerably, that the numbness had disappeared from his hand and that his gait was much improved. During a preceding two weeks of hot, humid weather he said that his symptoms had recurred, but they disappeared with cooler weather. Further examination on September 9 revealed a status similar to that on admission except for more marked difficulty in gait and a positive Romberg sign.

The literature is silent on transitory neurologic changes during artificial hyperthermia. Occurrence of such changes during hyperthermia from malaria and other biologic agents has been reported. However, in these reports there are to be considered the factor of the infectious agent and its effect on the nervous system.

Improvement in multiple sclerosis following hyperthermia as reported in the literature has consisted in diminution in the spastic syndrome, improvement in gait, recession of ataxia and tremors and amelioration of urinary retention. The spinal form seems to be more likely to improve than the cerebral type.

The case reported led us to make neurologic examinations during hyperpyrexia on other patients, with and without neurologic lesions. The most consistent finding was loss of deep tendon reflexes, this loss being transitory during the fever. Another patient with multiple sclerosis complained of weakness of the feet and hands and "numbness" during treatment. Examination showed disappearance of deep tendon reflexes (they were hyperactive before treatment), loss of ankle clonus, hypesthesia to all forms of sensation in the extremities and moderate reduction of motor power. Cases of other conditions are cited.

Physiologic and pathologic changes must occur in the nervous system to explain the preceding transitory findings. One cannot be sure whether they are based on transitory edema, hyperemia, anemia, anoxemia, alkalosis, increased or decreased blood flow, temporary thromboses or other physiologic and biologic factors. As far as permanent neurologic complications are concerned, pathologic changes undoubtedly have occurred to produce the symptoms and signs noted. The nervous system is susceptible to high temperatures. It is hoped that more neurologic examinations will be performed on patients receiving hyperthermia, not only because of academic interest but also because practical facts regarding the prevention of serious neurologic disorders might be discovered.

DISCUSSION

DR. I. S. WECHSLER: This is the first paper I know of which has reported careful studies of the neurologic manifestations resulting from hyperthermia. Isolated reports have appeared, but nothing as extensive. What interested me, aside from the proffered explanation of the clinical observations, was the haphazard treatment by hyperthermia of certain neurologic conditions. Evidently it is not a harmless procedure. Contrary to the opinion frequently expressed by eminent neurologists, I am not convinced of the value of hyperthermia in chronic degenerative diseases of the nervous system.

During a period of five years 72 patients with multiple sclerosis have been treated at the Mount Sinai Hospital. Fifty-two were treated with typhoid therapy; the temperature produced is not quite as high as that with the malaria treatment or electrohyperthermia, although it will rise to 104 F. Of the 52 patients, 28 have shown improvement. Four patients improved slightly; 20 did not improve. In other words, 54 per cent improved; 8 per cent improved slightly, and 37 per cent did not improve. Of 7 patients treated by artificial hyperthermia such as Dr. Collins uses, 4 improved and 3 did not. Again, in terms of percentages, 57 per cent improved, and 43 per cent did not improve. Thirteen patients were not treated with hyperthermia; in other words, they were not treated at all. Nine improved, and 4 did not; that is, 70 per cent of the untreated patients improved, as compared with 54 and 57 per cent treated by the typhoid and electrohyperthermia methods, respectively. It may be well to add that in all cases the improvement was essentially subjective. The neurologic signs did not change, but the patient said he felt better. On the other hand, of the patients who were unimproved, some became worse. The patients treated with hyperthermia were kept longer in the hospital than other patients, and it is a question whether time and rest, rather than the hyperthermia, were not the factors responsible.

Personally, I believe that until the etiology of a disease like multiple sclerosis is known, treatment by hyperthermia or, for that matter, by any other means, is a stab in the dark. If what Dr. Collins said is significant and his observations are confirmed in subsequent cases, hyperthermia not only will not be of benefit but may actually do damage. I wonder whether the treatment has any scientific basis and whether it is worth carrying out in practice except, of course, for purposes of study.

DR. WILLIAM B. SNOW: I approach the discussion from the point of view of the physical therapeutist. Dr. Collins has made a valuable contribution to the accumulative bulk of data associated with the subject of fever therapy. Unquestionably, the great majority of persons using this method have not routinely made neurologic examination of their patients during the treatment. The possible occurrence of irreversible reactions traceable to injuries to the spinal cord is impressive. Untoward results of fever therapy have been reported in the literature. However, there is little mention of such occurrences as Dr. Collins describes, and such events are probably unusual. Of far greater frequency are the results which have been traceable to cardiovascular collapse, cerebral compression, dehydration, failure of the heat-regulating mechanism and, last but not least, incompetent follow-up care of fever patients.

Fever therapy has passed the stage of random experimentation. From the standpoint of the therapeutist, the most important chord which Dr. Collins strikes is a sincere desire to avoid untoward results from fever therapy by the elimination of hazards.

Fever induced by typhoid, as has been demonstrated by DuBois and his associates, is far different from that induced by physical means. Injections of the typhoid bacillus cause interference with the normal heat-regulating mechanism, which is not present when fever is produced by physical means. In the latter case there is a constant attempt on the part of the patient's mechanism to dissipate the heat being brought to bear from external or internal sources, as the method may require. Consequently, until heat input exceeds heat output there is no satisfactory rise in temperature. The subjection of the patient to an environment of heat and high humidity disturbs the physiologic balance the least. Under these conditions, patients have a diminished requirement for sweating, with minimal disturbance of the chloride balance, less dehydration and less consequent reduction in plasma volume. Patients exposed to higher humidities from 85 to 100 per cent—also show little disturbance of $p_H$ values for the blood, less hyperventilation and diminished alkalosis. These factors are the most important consideration in fever therapy.

In connection with the symptoms which Dr. Collins has described, I have noted another interesting point. Often the earliest subjective symptom on the part of the patient with impending circulatory failure is the sensation of excessive heat in the fingers and toes. The temperature to which such patients are subjected does not exceed 120 F., which is easily tolerated when peripheral circulation is adequate.

DR. MARCUS NEUSTAEDTER: In 1930 I reported a series of 26 cases of neurosyphilis in which treatment with malaria was given, with fairly good results. In 1934, at the Neurological Hospital, Welfare Island, hyperpyrexia treatments were started in order to compare the results with those for malaria. Fifty-two patients with various types of neurosyphilis have been treated. One treatment has been given in each week, up to thirteen treatments, at a temperature of from 103 to 105 F. Of the 20 patients in this series who had received the full course of treatments, 10 improved—3 clinically and 7 only subjectively. Four patients with multiple sclerosis were treated; these showed no untoward effects, but no improvement.

I understand that in Dr. Collins' cases the hyperpyrexia treatment was given every other day, with serious and unpleasant after-effects. I wonder if the frequency of the treatments had something to do with it. In the case of a neurosyphilitic patient in my series the treatment was discontinued when the temperature reached 105 F.; it suddenly rose to 108 F., and the patient became pulseless; there was great difficulty in reviving him. It seems to me that it is better to induce hyperpyrexia once a week than every day. Why hurry? Like every other method, the treatment may be of some value if one is cautious and takes time.

DR. RALPH T. COLLINS: Regarding Dr. Neustaedter's statement concerning the frequency of treatment: As far as multiple sclerosis is concerned, I should like to state that since the hyperthermia service was established at the Neuro-

logical Institute in December 1935, there have been treated 14 patients with multiple sclerosis. All received two or three treatments a week, and in only 2 cases, which I reported tonight, were there untoward results. My colleagues and I do not give quinine during hyperthermia.

"CACHEXIA NERVOSA": A PSYCHONEUROTIC SIMMONDS' SYNDROME. DR. IRVING H. PARDEE.

Eight cases of severe emaciation, with recovery, are reported. The patients presented a syndrome of cachexia, amenorrhea, low basal metabolic rate and absence of estrogenic hormones, all evidencing a pluriglandular deficiency with marked similarity to Simmonds' disease, though differing from it strikingly in that there is no aging of the tissues, falling of the hair or uniform fatality. Because the old term anorexia nervosa does not describe either a characteristic symptom or a sign, it is suggested that "cachexia nervosa" be substituted.

The outstanding symptoms refer to the gastrointestinal tract; there are obsessions about food, refusal of it, anxiety, depression and a wealth of psychoneurotic manifestations, all of which make it a diagnostic entity outside the realm of organic disease. The treatment must be directed toward the maladjustments in the life of the patient, with an attempt to bring about readjustment to parents, sex life or marriage and to break the patients permanently from their adolescent fixations. With such common sense psychotherapy the patients are won back to a new interest and understanding.

DISCUSSION

DR. CLARENCE P. OBERNDORF: Dr. Pardee has presented a series of interesting cases in which he has called attention to the necessity for a differential diagnosis between pluriglandular and psychogenetically determined nutritional changes which may be confusing. Other investigators have called attention to the fact that at times complete atrophy of the pituitary gland occurs without the symptoms found in Simmonds' disease, implying that some factor other than atrophy of the gland must be responsible even for the symptoms in Simmonds' disease. From Dr. Pardee's observations, one might infer that this unknown factor is uniformly psychogenic.

In some of the cases which Dr. Pardee has described the condition closely resembles the refusal of food and pernicious vomiting associated with hysteria. The connection between the refusal of food and sexuality is recognized and is only a variation of the well known psychologic mechanism of displacement from below upward. It may be of interest to this audience that in 1913 the late Dr. H. W. Frink and I presented a paper on a similar topic before the Bellevue Alumni Association and Dr. James J. Putnam, professor of Neurology at Harvard University, the first academician in the United States to embrace psychoanalysis, lent us his support. He illustrated the ethical and moral significance which attaches to eating and sexuality by the following example: A friend of his, cruising in the South Sea Islands, entered a small bay which apparently no white men had hitherto visited. His men went ashore at noon to cook their meal. When the natives saw them cooking and eating in public they crept out of their huts and watched with great interest this extraordinary custom, which was forbidden among them. The meal ended, and the natives began to resume their work. The women went to a stream near the beach to wash and bathe nude. Then the crew stealthily went to watch the scene forbidden in their society. In other words, eating in public was a forbidden performance for the natives, as the open display of women was for the Caucasians.

Perhaps the most interesting point, which Dr. Pardee seems somewhat to have evaded, is why these patients should choose the gastrointestinal tract as the expression of a psychic conflict which is so prevalent. He has mentioned emotional immaturity, but such emotional conflicts toward mother and father are encountered in many patients suffering from schizophrenia or depressions, in

persons who cling to infantile habits and in those who show shyness and uncertainty and a tendency to retire. Why, then, do these patients use this particular form for expression of their rebellion? One must predicate that there is a congenital predisposition to oral sensitivity and that here one is concerned with an unconscious conversion to the negative of a desire to return to the maternal breast. If one assumes this, perhaps one may understand why these persons use the gastrointestinal-oral method for indicating their unresolved conflict.

When a patient has been suffering sufficiently long from refusal of food or vomiting, apparently an irreversible condition is established which the patient cannot restore to normal. This, I think, accounts for the persistence of the phenomenon and for the patient's inability to remedy it, even though he or she has a conscious desire to do so. Rather, I should paraphrase one of Dr. Pardee's sentences, namely, that these patients react at a vegetative level but certainly do not live at that level, for their thinking is at times remarkably clear and far from vegetative.

Another important point, and perhaps the reason for Dr. Pardee's presentation, is the therapeutic approach. Dr. Pardee has minimized the value of endocrine therapy, so often used in such cases, and has resorted to dietetic, persuasive and other psychotherapeutic measures. I agree with him in his general explanation of the phenomena of this condition, but I cannot acquiesce in the statement that when the reason is explained to the patients they will understand it because "they have not a leg to stand on." As a matter of fact, they usually continue to lie flat on their backs. I am inclined to think that these patients need not new legs but an understanding of how to use better the legs that they have. How that can be attained is another question. Dr. Pardee avoided it by saying that he will not be drawn into a controversy concerning psychoanalysis.

In cases in which the family's reactions are so vitally bound up with the patient's disease the suggestion of intensive psychotherapy is deeply resented by the parents and by the patient as well. Some indirect method such as Dr. Pardee uses, with an explanation on a psychoanalytic basis, seems the only possible initial approach because even if the patient and parents acquiesce in psychotherapy there is constant interference by the latter. After the patient has shown the first improvement and has reorganized his eating habits, a penetrating investigation along psychoanalytic lines should be more permanently effective.

Dr. A. A. Brill: The impression that I received from Dr. Pardee's paper is pleasant. He is the first endocrinologist to state that the glandular conditions in these cases are secondary to the psychogenetic. I have seen a number of cases similar to those which Dr. Pardee described. In some of them the condition appeared to be dysglandular and had been treated by endocrinologists long before I saw the patients. Most of the patients were mildly schizophrenic; some had mixed disturbances of the schizoid-manic type. As Dr. Pardee read his paper I thought of 6 patients whom I have observed recently. I agree with everything that Dr. Pardee said about his findings, as well as with the explanations given by Dr. Oberndorf. These patients are difficult to manage; most of them are more or less inaccessible. In only 1 of the cases I mentioned was the treatment successful. I have not heard from the patient for the last year or so; after treatment she married, and all had been going well for about three years; however, she retained her infantile type of personality.

I subjected patients with anorexia nervosa to as deep an analysis as I could—that is, when the patient was accessible. I have always considered the condition as a form of psychic suicide. The symptom is often found in young children. I have reported some cases. Dr. Friedjung, of Vienna, expressed full agreement with me that anorexia nervosa in children is a form of psychic suicide. The adult patients with this syndrome are all infantile in makeup.

I believe that the prognosis for this condition is rather unfavorable, especially in patients with a schizoid makeup. As was stated by Dr. Oberndorf, family interference contributes much to the failures. Thus, one of my patients was the sister of a physician. I advised him to leave her alone, not to watch her—if she

did not eat enough he was not to urge her and argue with her. However, he could not keep his promise for more than a day or so. Sometimes he telephoned me five or six times a day, saying that she had not touched anything and urging that something be done. I had similar experiences with the parents in almost all cases. I believe that most of the patients are of a psychotic type. If not pronouncedly schizophrenic, they are nearly so. Few of them are psychoneurotic, but they are all difficult to handle.

DR. EUGEN KAHN, New Haven, Conn.: One may say that food and sex are two aspects of biologic necessity and that there are people who avoid or dismiss these functions, which may be culturally tabooed. In this there is a thoroughly "spiteful" attitude. This brings me directly to what Dr. Brill said about anorexia in children who do not eat for spite. One sees all manner of difficulties between these children and their parents. In this group of patients with anorexia there may be a certain type of personality makeup. If I dare venture a guess, this type may be in certain contrast to a type which has been found among patients suffering from ulcerative colitis. There are various sorts of ulcerative colitis, but I have seen more than a few patients in whom the colitis developed on an emotional basis. I have found without any notable exception that there is a tremendous attachment to the mother from the beginning, which develops into a dramatic situation when the patients marry. I have seen, furthermore, that these patients do not "stick to their guns." They are not spiteful; they let go, give up. They seem to punish themselves through their bodies; here I agree once more with Dr. Brill—not too rarely they seem to aim at some sort of suicide.

DR. BELA MITTELMANN: In confirmation of Dr. Pardee's observations, I may say that at the New York Hospital in the last few years all cases in which the condition was diagnosed as Simmonds' disease proved to be instances of "cachexia nervosa." The patients were followed by Dr. H. B. Richardson. All suffered from severe malnutrition as a result of disturbed appetite, gastrointestinal discomfort and diminished intake of food. These symptoms were connected with severe emotional conflicts.

In the light of these experiences, the question may be raised whether the syndrome of pituitary cachexia in the strict sense exists in human beings. I wish to ask Dr. Pardee how many patients with genuine Simmonds' cachexia he has seen during the period in which he observed the present series. I wish to ask further whether it has been possible to produce in animals, by removal of the pituitary gland, the symptoms of Simmonds' disease? Dr. Pardee has shown convincingly what profound effect prolonged malnutrition had on the endocrine functions in his patients. There is at least a possibility that such disturbances accompany reversible anatomic changes in the glands affected. My question, then, is: What anatomic changes have been observed in the hypophyses of animals which died of starvation? I wish to make one remark about the prognosis in cases of "cachexia nervosa." All patients observed by Dr. Richardson recovered with psychotherapy and hospital care; they gained weight; their metabolism rose, and in women the menstrual periods became regular.

DR. IRVING H. PARDEE: I was particularly interested in Dr. Oberndorfs explanation of a desire to return to the breast as a factor in this condition. Perhaps that is one reason that the patients like fluids so much. I have rarely seen vomiting in these cases. It has occurred in some of the cases reported in the literature, but in none that I have reported. I know that Dr. Oberndorf was not drawing any conclusions as to psychogenic atrophy of the pituitary, but I feel sure that the functional involvement of the pituitary in cases of cachexia nervosa is a problem of nutrition more than of anything else. Dr. Oberndorf was also keen in emphasizing the difficulty in getting the parents to cooperate in these cases. That is universally true, and I presume it is one of the main reasons that the patients are sick.

Dr. Brill, with his usual insight, put his finger on the point of this problem. Here is an endocrinologist presuming to say that this condition is psychogenic.

Thank you for saying it, Dr. Brill. I found that endocrine therapy was of no use, and so I had to make some other approach. I think one must look on this disturbance as different from more severe mental disease, such as dementia praecox and other psychoses in which malnutrition and cachexia from starvation take place. This syndrome is much less severe and, for that reason, recovery is more usual. A condition of this type is practically always curable, with proper handling; 80 or 90 per cent of the patients whose cases are reported in the literature recovered, though in rare instances they have starved themselves to death.

I think there is a close relationship in these cases to the attitude that children have in refusing food. The mother says: "Mary, eat your porridge," and Mary thinks: "Why can't I eat it without Mother telling me to?" The same attitude pyramids itself to a point at which there is absolute refusal of food.

I appreciate the remarks by Dr. Kahn and Dr. Mittelmann. I have seen 1 case of true Simmonds' disease in the last ten years; so it is a rare syndrome. As to whether it is possible to induce pituitary cachexia experimentally in animals: Dr. P. D. Smith has done so by producing lesions in the pituitary. Lesions have been produced in animals not only in the pituitary but also in the basal region above the gland by interfering with the supraoptic-pituitary tract, with marked cachexia as a result. Therefore, one must accept the fact, and I should like to emphasize again that in Simmonds' disease the symptoms are those of a progressive pluriglandular deficiency attended by atrophy of the pituitary, gonads, thyroid and other endocrine glands, while anorexia or cachexia nervosa is a functional disorder, dependent on certain psychogenic mechanisms resulting in loss of desire for food, with malnutrition and secondary pluriglandular disturbances, which recovers with return of nutrition, usually without endocrine therapy.

THE PROBLEM OF MARIHUANA IN PSYCHIATRY. DR. WALTER BROMBERG.

The rise of popular interest in the influence of marihuana on mental illness, crime and drug addiction during the last five years in many quarters of the United States points to the usefulness of a psychiatric review of the problem.

Thirty-one cases of mental illness following the use of marihuana (marihuana psychosis), seen at the psychiatric division of the Bellevue Hospital, are reported, including 11 previously reported by me (*Am. J. Psychiat.* **91**:303 [Sept.] 1934). These are classified as instances of: (1) acute intoxication, lasting from hours to days (14 cases), and (2) toxic psychoses, lasting from weeks to months (17 cases); often the toxic picture is superimposed on a basic psychopathic state, such as schizophrenia.

Marihuana is the name of a nonmedicinal preparation of the hemp plant (Cannabis sativa), which contains the drug cannabis. The effects of marihuana are similar to those described in Europe from hashish, which is made from the plant Cannabis indica. The common method of use is in cigaret form. Smoking produces characteristic symptoms involving the emotional sphere, the subjective world, feelings of bodily change and motility in varying degrees in different persons.

Anxiety and apprehension are first aroused. These emotional experiences are vital to the stimulation of suicidal attempts, panic reactions and transient depressions. The inner fear of bodily dissolution is in response to somatic changes induced by the drug. These reactions are observed in both the acute intoxication and the toxic psychosis. Mental confusion with visual illusions and hallucinations is present in both groups. Motility disorders, such as excitement, restlessness and aggression, are also present in both the acute intoxication and the toxic psychosis. The duration of these symptoms varies in each mental state.

The basic personality of the smoker appears to be a vital factor in the development of marihuana psychosis. Countless persons use marihuana without the development of an observable mental disturbance. Often the drug represents the incipient stage of a functional psychosis. In such cases there appears to be an intimate relation between the dissociation in the patient's personality and the sub-

jective effects of the drug, which tend to widen this dissociation and produce a psychosis. In cases of acute intoxication there is no permanent effect observable by psychiatric examination after the effects wear off.

In the Court of General Sessions, which handles the felonies for New York County, over a period of five and one-half years 200 offenders were convicted of drug addiction or found to be users of drugs. Of these, 67 were users of marihuana. Analysis of this group revealed only 3 who were constant users of the drug. In only 9 cases did the criminal record start with the drug charge.

In the Court of Special Sessions, which handles the misdemeanors for New York County, in a six year period there were 6,000 convictions for addiction to drugs; of these, about 540 persons used marihuana. Only a few progressed from use of drugs to other crimes. In other words, early use of marihuana apparently did not predispose to crime. There was no positive relation between violent crime and the use of marihuana. In my series there were no cases of murder or sexual offenses occurring among users of marihuana.

The lack of increasing tolerance and the absence of withdrawal symptoms on cessation of the use of the drug argue against marihuana being habit forming. Offenders all agreed that in their personal experience it is not habit forming. At most, it can be said that the use of marihuana is a "sensual addiction" in the service of hedonistic elements of the personality.

### DISCUSSION

HON. FREDERICK L. HAKENBURG: I agree with Dr. Bromberg that users of Cannabis indica do not become major criminals. In my experience of five years as judge at the Court of Special Sessions, where these cases are handled from the criminal standpoint, I have found 2 or 3 instances in which I thought that the use of marihuana led to crimes of impairing the morals of a minor and some cases of assault based on sexual desires. I may be mistaken, because it is almost impossible to gage the effect of Cannabis indica by the time the offender comes to the court. Dr. Bromberg is entirely correct when he states that the effect of this drug wears off in two days. The cases do not come up in court until three or four days after the arrest. By that time one cannot trace the effects of the drug on the mental condition at the time of commission of the crime. This, in itself, is a problem.

The court has an additional problem, owing to the rapid growth in the use of Cannabis indica. Heroin (diacetyl morphine), morphine and opium cost a great deal. Some of the supply is smuggled. The business is big. One can trace it; one can watch it. But Cannabis indica is a hemp plant that grows anywhere. It is cheap. In my own limited experience, I recall a situation in Brooklyn in which the police discovered by accident a plot 100 by 40 feet (30.5 by 12 meters) in which Cannabis was being grown for the purpose of making "reefers." If the entire crop had been collected, $7,000 or $8,000 would have been realized.

"Reefers," the cigarets, are sold for 10 cents each. In a good place in Harlem they will cost 20 cents. Another problem is the difficulty of identifying these cigarets. They look like ordinary cigarets to a police officer.

They are running "reefer parties" in Harlem, and the habit is spreading outside. Fifteen or 20 people sit in a circle; a Cannabis indica cigaret is passed around, and everybody takes a puff. I think that this is important from the criminal point of view. It confirms my own conviction that 90 per cent of all crime arises from economic depression. It is something one may have to look into and try to meet. The use of these cigarets is spreading. I had information that people were peddling reefers in front of one of the high schools in Manhattan, selling them to boys and girls 15 or 16 years old. In that case the persons who were peddling reefers to children were apprehended.

Dr. Bromberg did not give much that I expected. I should like to know about a cure. Apparently, no one knows what to do about that. Medical science can cope with morphine and many other drugs. Often, after a man is released as cured, he returns to the habit after a while but that, again, is due to frustration,

lack of will power or economic factors. As for Cannabis indica, I have talked to physicians, police officers, social workers and others; no one knows what to do about it. When marihuana addicts come before me I do not know whether they are users or how they are affected, because by the time they are arraigned the effects have disappeared. I have to deal with the case simply as one of a crime, as the legislature tells me to. Still, it is a problem for the medical profession. If the use of marihuana is not a crime, imprisonment is not an answer; probation is not an answer. I have tried this method, and it was not successful.

As to the suggestion that marihuana leads to serious crimes: I had the first light on that question from a police officer stationed at Battery Park. A good many sailors from the sailors' home walk about Battery Park and West and South streets; for some time, reefers have been sold to them. The police officer told me that these smokers are not a menace as far as serious crimes, such as assaults and robberies, are concerned; they are just a nuisance. How much that is worth to you, Dr. Bromberg, in your work I do not know. I can arrange for you to talk to the police officer if you wish. He observes many of these smokers every night.

Dr. Alexander Gettler: Since I am a chemist, a toxicologist, it is impossible for me to discuss Dr. Bromberg's paper from a neurologic standpoint. From a toxicologic point of view, deaths from acute marihuana poisoning are rare—in fact, I have never known of a case in which death resulted from the taking of marihuana resin (the lethal dose is large—from 1 to 5 Gm.), and people do not die from smoking marihuana cigarets. In cases of death from acute intoxication, when the marihuana resin was taken per os, one can readily identify the active principle; in the case of cigaret smokers, however, little of it enters the circulation, and most of that is destroyed. Traces of cannabinol, the active principle, are hard to detect; at present I am trying to work out methods by which one can do that.

I shall give briefly an idea of how one can identify by microscopic and chemical means, first, the plant, second, the drug and, third, the cigaret.

(Lantern slides were shown.)

The plant Cannabis indica, usually about 4 to 6 feet (120 to 180 cm.) high, is sometimes as much as 16 feet (490 cm.); it is a herbaceous annual and matures in about three months. The stalk is one-half to 2 inches (1.27 to 5 cm.) in thickness, with a fibrous four-cornered ridge. There are numerous short branches. The leaves are compound and palmate and usually have five, seven, nine or eleven lobes. They are serrated, and under the microscope the veins are characteristic.

The following test is specific for marihuana. When the material in the cigaret or the drug is spread on a microscopic slide and moistened with water and a cover glass is placed on it generalized warty blebs will be revealed. These are characteristic of the upper surface of marihuana leaves. On the under side the hairs are much longer and finer and have a fuzzy appearance. On the edges of the leaves there are barblike structures which resemble cat's claws.

The marihuana cigarets are always rolled individually, in contrast to tobacco cigarets, which are machine rolled. In chemical testing, the resin is first extracted with any one of the immiscible solvents, such as ether, ethyl acetate or purified petroleum benzin U. S. P. The solvent in the extracted material is then evaporated; the resinous residue is then tested. In the United States the alkali and acid Beam test is used. In this one applies to the residue an alcoholic solution either of potassium hydroxide or of hydrochloric acid; a violet or a red color, respectively, should develop. The Government uses this test, but it is not reliable. Sometimes one obtains the color reaction, and sometimes one does not. In a paper published recently (Duquenois, P., and Hassan Negm Moustapha: *J. Egyptian M. A.* **21**:224, 1938) a much better test is described. It can be performed with a cigaret in about two minutes. The cigaret material is extracted with purified petroleum benzin, as previously described. The extract is placed on a watch glass and allowed to evaporate. The residue is then treated with a few drops of the following reagent: 300 parts of ethyl alcohol, 7 parts of vanillin and 1 part

of acetaldehyde, followed by a few drops of concentrated hydrochloric acid. A green, and then a beautiful blue, reaction develops. The test has been tried on 60 drugs, and none but marihuana gives this reaction. It can be used for quantitative determination as well.

Dr. Bromberg has mentioned three or four names by which marihuana is known. I have found in the literature thirty-one names for the products of this plant. From the flowering tops and leaves of the plant there is obtained a drug called cannabine, of which the active principle constitutes about 15 or 20 per cent. This active principle is called cannabinol. It is a red oil, which is soluble in organic solvents and can be distilled. The formula for this oil is $C_{21}H_{30}O_2$. It is not an alkaloid. It contains two benzene radicals, with oxygen in an ether-like combination.

DR. EUGEN KAHN, New Haven, Conn.: I, with others, had the opportunity to see experiments carried out by Drs. Kant and Krapf in Munich. We observed a young man in the wards who, we were told, had been smoking two reefers. We first thought his case was one of marihuana intoxication, but he proved to be schizophrenic. What impressed me was the age of Dr. Bromberg's patients. The average age was 25, with a range from 16 to 38. I do not pretend to know what this indicates, but I think it may mean something. It may be of significance, too, that among the 30 patients there were only 4 women.

It was interesting to note that Dr. Bromberg seems to have difficulties, as all have, in differentiating between hashish psychosis and schizophrenic conditions. It is this problem about which I shall make a few, possibly incautious, remarks. It is necessary to note that Dr. Bromberg emphasized the role of anxiety in his 30 cases. This is true in cases of intoxication as well as in those of toxic psychosis. He emphasized the role of psychopathic personalities in this group. He said that few, if any, cyclothymic persons smoke hashish. He also said that patients with manic-depressive conditions are doubtless in a minority. This seems to indicate that persons with psychopathic trends, anxious, tense, insecure—not pyknophilic or cyclothymic—persons, formed a majority of Dr. Bromberg's patients. I speak only of his patients; I cannot speak for the thousands of people who may be smoking hashish. The anxious, insecure people seem to pass into the acute or prolonged hashish conditions, experiencing, in addition to their original anxiety, anxiety due to the drug. Here it is important to cite Dr. Bromberg's observations. He said that emotional reactions to the symptoms are of an importance equal to that of the psychologic factors. Perhaps this is one of the most important considerations, for the emotional element may be a powerful factor in driving people to smoke marihuana and to use other drugs. There is still the resemblance between the experiences of some hashish smokers and those of schizophrenic patients. In a number of instances at least the personality makeup of hashish smokers shows a definite resemblance to that of schizophrenic patients. If one thinks, as some do, tentatively, that there is a cyclothymic personality with predominant pyknophilic traits and, on the other hand, a noncyclothymic personality, one may say that one pyknophilic quality is the ability to bend, to be elastic, whereas the more leptophilic person is not possessed of this ability. Such persons are rigid, and they break—break under the effect of intoxication, as well as other conditions, such as schizophrenia.

A suggestion came to me as I was reading Dr. Bromberg's paper. If one says there are personalities which are elastic and personalities which are rigid, one makes an attempt to formulate a complex problem in as few words as possible. What is the matter with people? I begin to think there are some normal personalities left; there are still people who can adjust themselves to situations. On the other hand, there seem to be people who are unable to accept any actual situation, who in all situations have to create one for themselves. I wonder if Dr. Pardee's patients might not be included here, too.

There are people who must create a situation in order to be able to carry on. The fact that these persons create their own situation does not mean that they are fully able to run away from the actual situation as the so-called normal person

would see it, but they are caught between it and the one they have created. Now and then they break, and it is of social and psychiatric importance—there is a break between person and situation, and then hell is loose. Why it occurs in the form of a so-called schizophrenic process or a hashish intoxication is hard to answer. I grant that all hashish smokers—and Dr. Bromberg has made this clear—will not experience intoxication in the same way. However, some have queer syndromes that remind one as a clinician of schizophrenic pictures. I suppose that something may be amiss in the personality makeup of these persons. They are never able fully to accept an actual situation.

During the last few years there has been much discussion of the experience of time, to which Dr. Bromberg has alluded in his paper and which enters rather significantly into what I choose to call the break between the person and the situation. One makes a mistake if he speaks of reality in the sense of the present. There is no present in experience. One may live in the present; one may function in the present, if you wish, but there is no experience of the very present. The moment flees and is gone before one experiences it. One experiences in the future, but one acts as if he were experiencing in the present. Even if one looks back, experiences are a sort of anticipation. One never experiences in the present moment. People with less elastic qualities experience a lengthening of time. It is as if they were not able to fall in with fleeing time and with the experience which is necessarily always an experience of the future. There are differences, I dare say, in this respect between persons with more and those with less elasticity, because the latter do not seem to be able to accept the fact that there is no present in experience, but only the future. I imagine that in one way or another this fact is one of the most important sources of what is called anxiety.

Dr. Walter Bromberg: I remember that three months ago, before he read my paper, Judge Hakenburg said physicians knew nothing of this subject; he says the same thing now. What I attempted was to clear the ground in regard to the psychiatric effects of marihuana. When one has cleared the ground, one must consider what to do about it. Whether one can legislate the hedonistic elements of the personality is essentially a problem of social psychology. It is neither judicial nor medical. I can only point to education as a possible aid in teaching people to secure the most out of their bodily sensations without the aid of drugs.

Dr. Kahn's discussion of the distortion of personality and time is apt. The question of anxiety in marihuana conditions is interesting in that there is almost a specific difference between the effect on the personality of alcohol and that of cannabis. Alcohol is related to basic (unconscious) inadequacy and homosexuality, while cannabis has to do with the inner perception of the body model. I pointed to these two divergencies in the clinical material—cannabis distorts the body image; alcohol distorts or helps the psychosexuality. The difference between the toxic psychoses and the intoxications is not important except that it aids in a prognostic understanding of the problem.

Dr. Gettler's exposition was very clear and presents the biochemical aspects, which are difficult to obtain anywhere else, even in textbooks.

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## PHILADELPHIA NEUROLOGICAL SOCIETY

J. C. Yaskin, M.D., *President, in the Chair*

*Regular Meeting, Oct. 28, 1938*

Treatment of Meningitis with Sulfanilamide. Dr. Josephine B. Neal, New York (by invitation).

*Meningococcic Meningitis.*—Wide differences of opinion in regard to the proper use of serum persist. There are several reasons for this: the presence or absence

of meningococcemia, the use at times of serums of low potency, the recent introduction of antitoxin, the theory that serum should be given intravenously only and the use of sulfanilamide or its derivative combined with serum or alone. I believe in the conservative use of serum by the intraspinal route alone, unless there is definite meningococcemia. It is my impression that sulfanilamide is a useful adjuvant to the serum in cases of meningitis and that it may replace serum in treating meningococcemia, and possibly meningitis.

*Other Forms of Purulent Meningitis.*—The treatment of other forms of purulent meningitis depends on the etiologic agent and the relation to a primary focus. In the majority of these forms treatment is still inadequate. The use of phage or sulfanilamide is worthy of trial in cases of meningitis due to organisms of the colon-typhoid group, the staphylococcus or Bacillus pyocyaneus. A combination of serum and sulfanilamide is indicated in cases of meningitis due to the Pfeiffer bacillus, but the results are disappointing. Fothergill recommended the intraspinal use of fresh human complement with each dose of serum. Pneumococcic meningitis was uniformly fatal in my experience until I began the use of sulfanilamide. Since, I have observed 42 cases in 7 of which recovery occurred. Finland has suggested a method of treatment, using specific serum intravenously, sulfanilamide in large doses, frequent spinal drainage and the intraspinal injection of from 5 to 10 cc. of the patient's own serum, if it contains antibodies, or if not, of from 5 to 10 cc. of human serum and from 0.5 to 1 cc. of specific serum.

Recently, a new derivative of sulfanilamide with a pyridine radical (2-[para-aminobenzenesulfonamido] pyridine), known as sulfapyridine or "M. & B. 693," has been described and recommended, especially for pneumococcic infections. It is a rather insoluble powder and must be given orally. It has been used too short a time for definite conclusions as to its relative value. The fatality rate of hemolytic streptococcic meningitis has been reduced from more than 95 per cent to about 20 per cent by the use of sulfanilamide. My colleagues and I have listed 35 cases in 28 of which there was recovery.

In all these forms of meningitis it is important to remove the focus of infection and to drain thoroughly the subarachnoid space.

The derivative of sulfanilamide that I have used most is neoprontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonic acid). I have found this preparation at least as effective as and less toxic than sulfanilamide.

DISCUSSION

DR. H. F. FLIPPIN: When a general practitioner is asked to discuss a paper of such high caliber as this at a meeting of neurologists, he realizes that he is treading on uncertain ground. Those who have been interested in the sulfanilamide treatment of streptococcic infections realize that the work which Dr. Neal has just presented is undoubtedly one of the greatest contributions to modern medicine since sulfanilamide was introduced several years ago. Dr. Neal has been indeed modest in her presentation, as she has estimated the mortality rate in her series as approximately 20 per cent. As will be recalled, in case 7 the patient was only 2 years of age, and death resulted from lateral sinus thrombosis; in another case a subdural abscess was present; in 3 cases treatment was instituted for only about twelve hours. When these 5 cases are considered, the mortality rate could be considered as 10 per cent.

As general practitioners, my colleagues and I have been interested in several factors, particularly the intraspinal use of serum. It has been our experience that the use of sulfanilamide intraspinally has an irritating effect on the tissues of the membrane. During the past few years we have used, with apparent success, lyophilized human convalescent serum intraspinally in order to supply complement to the spinal fluid. I wish to ask Dr. Neal if she has had any experience with this form of therapy.

Focal infection, which Dr. Neal has stressed, has been a factor in the treatment of meningitis. Today, nose and throat specialists do not fear operating procedures

as they did in the past, and I am confident that the eradication of foci, together with the use of sulfanilamide, is responsible for recent successes.

Dr. Neal also mentioned a new drug, sulfapyridine (2-[paraaminobenzenesulfonamido] pyridine). This sulfanilamide compound has been used in England for the past six months with apparent success in streptococcic, pneumococcic and meningococcic infections. During the past few weeks I have had occasion to observe 2 patients with pneumococcic meningitis who were treated with this new drug. In both cases there was marked improvement in the meningeal symptoms and spinal fluid findings. One patient recovered; the other died, seven days after the treatment had been discontinued, of diabetic complications. At autopsy there was no evidence of meningeal involvement except for a small patch of resolving meningitis on the cortex of the brain. At this time it is my belief that this new compound, which is much less toxic and just as efficacious in treatment of streptococcic, meningococcic and gonococcic infections, and more so in pneumococcic infections, will eventually supplant the use of sulfanilamide.

DR. M. S. ERSNER: I heartily agree with Dr. Neal that sulfanilamide and its component groups are a godsend in the therapeusis of meningitis, especially from an otorhinologic standpoint. Until the advent of sulfanilamide few patients survived streptococcic meningitis. In 1930, in a review of the literature on cases of recovery from this disease, I found only 58 instances. The same year I had 2 cases of recovery from streptococcic meningitis; at that time I attributed the survival of these patients to chemotherapy through the internal carotid artery. Although these patients are alive today, I believe that their recovery was incidental rather than due to rational treatment.

One of the most essential factors in the successful termination of meningitis is the removal of the primary focus. I am glad that Dr. Neal stressed this fact, and I am firmly convinced that in all cases of otitic meningitis prior to the use of sulfanilamide in which the illness ended in recovery, early elimination of the primary focus was responsible. I hope that neurologists will agree with me in this statement.

In 1938, mastoiditis was infrequent throughout the country, and I ascribe its rarity to the early administration of sulfanilamide and its effect on the organisms. However, in the cases in which operation was performed interesting clinical and pathologic findings were revealed. The classic signs and symptoms of mastoiditis were absent. There was no sepsis, pain, fever or other marked manifestation of mastoiditis. However, the operative observations disclosed that the tissues were cyanotic and edematous, and bony erosions over vital structures were prevalent. These changes were out of proportion and were not consistent with the absence of the classic symptoms. It was not uncommon to observe perisinal and epidural abscesses. Therefore, mastoiditis and sinusitis without septic symptoms may occur when sulfanilamide is administered; in many cases, however, halisteresis continues, and the clinician is caught unaware when a catastrophe occurs.

Then, again, sulfanilamide often produces sustained fever, which does not subside until the drug is completely eliminated from the system. Sulfanilamide often produces grave complications, such as hemolytic jaundice, agranulocytosis and hematuria. On the other hand, I am happy to report the recovery of 6 patients with meningitis in the past year.

I wish to emphasize the importance of the following: (1) removal of the primary focus; (2) administration of sulfanilamide and its derivatives; (3) frequent blood transfusions; (4) search for suppuration of the temporal bone or one or more of the sinuses as the primary focus and its eradication; (5) watch for complications, which are often produced by the drug itself rather than by the infection.

DR. H. L. GOLDBURGH: May I ask Dr. Neal whether she considers the concentration of sulfanilamide in the blood to be the determining factor in dosage? Are concentrations above 12 mg. per hundred cubic centimeters more efficacious?

From an internist's point of view, I wish to emphasize the matter of acidosis. Some concentrate on the treatment of the infection with sulfanilamide and forget the associated biochemical changes induced by the drug.

In a case of pneumococcic meningitis, type 17, I gave sufficient sulfanilamide to keep the concentration in the blood up to 17.6 mg. per hundred cubic centimeters. The pneumococcemia was eliminated, with clinical and laboratory evidences of eradication of the meningitis. The carbon dioxide combining power was 30 volumes per cent. Sodium bicarbonate and a sixth-molar solution of sodium lactate were given intravenously in sufficient doses to overcome the acidosis. The latter persisted in spite of attempts at alkalinization and the administration of dextrose. Jaundice appeared, and the size of the liver decreased. Autopsy revealed atrophy of the liver, the weight being 750 Gm., with depletion of fat and glycogen. The kidneys showed marked damage. There is no doubt that once acidosis is allowed to evolve, whether it is the cause or the result of damage to the liver and kidneys, treatment may be of no avail.

DR. JOSEPHINE B. NEAL: I never have used lyophilized human convalescent serum in conjunction with sulfanilamide, and I have not had much experience in using human serum as complement in cases of meningitis, as has been recommended by Fothergill and Finland, in Boston. Fothergill and Finland have done a great deal of valuable experimental and clinical work on influenzal and pneumococcic meningitis, and I think therefore that the use of human serum as a complement in treatment of influenzal and pneumococcic meningitis should be tried.

It is not impossible that an occasional patient may have a severe toxic reaction with the use of neoprontosil, though, judging from my experience, such a reaction is extremely rare. With neoprontosil one will not find nearly as high a concentration in the blood or in the spinal fluid as one would if large doses of sulfanilamide were used. Yet, as I say, I obtain results that seem satisfactory by using neoprontosil in moderate doses.

It is important, in treating patients with sulfanilamide or its derivatives, to use the alkali immediately. In the case which was discussed, that of the patient with diabetes, one was dealing with an unusual situation, and it is probable that no matter how much alkali had been given the result would have been the same. I think one must attribute death to the diabetes and not to the infection. In fact, is it not true that diabetic patients fare badly with severe acute infections?

In cases of meningitis of any form, I usually continue to make lumbar punctures every day for a short time during convalescence, and I examine the fluids carefully to see that the organism is not returning. I use serum intraspinally in any case of meningitis in which a specific serum is available.

Judging from the reports, it is my opinion that when good results in treatment of meningococcic meningitis follow the intravenous use only of large doses of serum septicemia dominates the picture. Now sulfanilamide also is being used, and, of course, one knows that this chemical reaches the spinal fluid in a fairly high degree of concentration. One knows that neoprontosil does also. There are two reasons that I have used neoprontosil intraspinally: first, to raise the neoprontosil content in the spinal fluid. I realize this may not be necessary, but it can do no harm. Second, I like to drain the spinal canal thoroughly, and I think the patient is more comfortable if one replaces the fluid with some solution after removal of 40 or 50 cc. or more.

I have never used methylthionine chloride with sulfanilamide. Many years ago I did use it intraspinally, without results. I am not able to answer the question that Dr. Ersner raised in regard to epidural abscesses and the different kinds of tissue reactions in the region of a diseased mastoid following the use of sulfanilamide. I can hardly believe that sulfanilamide thickens the dura. It does not seem to have an irritating effect. A possible explanation might be that the administration of sulfanilamide has resulted in the organism penetrating more slowly through the mastoid to the meninges, with a different inflammatory reaction than would take place if its progress were not delayed by the action of sulfanilamide.

I wish to emphasize again how important it is to remove foci of infection. My experience seems to show that before the use of sulfanilamide it was possible in this way in a certain number of cases to prevent serous meningitis from progressing to a bacterial meningitis. Before the use of sulfanilamide, there were in my experience a few, 10 or 15, cases of recovery from hemolytic streptococcic meningitis in which the period during which the spinal fluid cultures were positive was sufficiently long that there seemed to have been more than a transient invasion of the meninges. One must remember that in cases of meningitis, as in those of other severe infections, there are always two imponderable factors with which one has to deal. One is the resistance the patient has or is able to acquire, and the other is the virulence and extent of the infection.

SULFANILAMIDE IN TREATMENT OF EXPERIMENTAL HEMOLYTIC STREPTOCOCCIC MENINGITIS. DR. JOHN S. LOCKWOOD (by invitation).

Meningitis was produced in white rats by injecting hemolytic streptococci through a trephine opening in the skull. Nineteen animals serving as controls died in an average of 2.23 days. Three animals that were given 150 mg. of sulfanilamide by stomach tube once a day died after a similar interval, but 1 survived. Eight of 14 animals given sulfanilamide, 75 mg. twice daily, survived, and the other 6 lived for an average of 6.8 days. Cultures of the blood obtained at autopsy showed that 80 per cent of animals used as controls showed septicemia, as compared with 11 per cent of treated animals. Conspicuous differences between the two groups were demonstrated by histologic study of material removed at autopsy from the brains and meninges of the animals: (1) There were fewer free streptococci in the exudates of treated animals; (2) none of the treated animals showed evidence of bacterial invasion of the cerebral cortex, as compared with an incidence of this finding of 63 per cent for the untreated group. Spread to the spinal meninges was present in 57 per cent of the controls and in 25 per cent of the treated animals which died. Localized abscesses of the brain of microscopic size were observed in 2 of the treated animals dying subsequent to withdrawal of the drug on the fifth day. Sulfanilamide administered by mouth appeared to be an effective agent in preventing the invasive complications of hemolytic streptococcic meningitis in rats, particularly if the drug was given in divided doses so as to provide a sustained level of the drug in the tissues.

DISCUSSION

DR. L. P. HANSEN: I have not personally had any experience with smaller animals in connection with studies of sulfanilamide, but my experience at the Jefferson Medical College has been with a variety of different types of infections. I have been impressed with recent papers by Dr. Neal (The Treatment of Acute Infections of the Central Nervous System with Sulfanilamide, *J. A. M. A.* **111:** 1353 [Oct. 8] 1938) and others in which they reported cures of pneumococcic and influenzal meningitis by maintaining levels of sulfanilamide in the blood of from 25 to 35 mg. per hundred cubic centimeters. No reference, however, was made to the amount of drug that was administered to maintain such high levels. In connection with ths problem, Query (Pneumococcus Type VII Meningitis, Treated with Sulfanilamide and Specific Serum, with Recovery, *J. A. M. A.* **111:**1373 [Oct. 8] 1938) reported a case in which he used successfully large doses, approximately 20 Gm. per day. The mental condition of the patient became such that the drug could no longer be administered orally, but it was continued by injection at the rate of about 5 Gm. per day until the mental condition changed and improvement progressed so that larger doses could again be given by mouth. The maximum concentration of the drug in the blood under those conditions was 26 mg. per hundred cubic centimeters. I wonder what doses were used to produce and maintain the higher levels in the blood indicated by the other workers.

I have not had any experience in studying levels in the blood with intakes higher than from 5 to 6 Gm. per day. I shall show slides to illustrate variations

in concentration and other facts relative to sulfanilamide therapy in man. These slides indicate the date of obtaining the specimen and the analysis, the date of the beginning of treatment, the interval since the last dose was taken, the intake per day, the fraction of the drug which remains unchanged and the fraction which is conjugated and the relative distribution in the blood and in the plasma. All these factors give emphasis to the complex picture of a given blood level. For example, with widely different levels of intake in the same and in different patients one may find approximately the same concentration of the drug in the blood, even though the time intervals since the last dose are virtually the same and the date of the beginning of treatment is sufficiently removed that one may reasonably assume a certain balance between tissue concentration and a given intake level.

In conclusion, I may mention that I have made studies on rabbits with the idea of determining what concentration in the blood one will secure with different doses. The maximum level attained with an intake of 1 Gm. per kilogram of body weight per day, in two doses, is 60 + mg. per hundred cubic centimeters. How that would compare with the value for the human subject I am unable to say, because I have not had the opportunity to study high intakes in patients.

DR. J. C. YASKIN: I wish to ask Dr. Lockwood if the histologic studies have shown the white matter in the brain to be involved as well as the cortex. The two practical points that one gains from these two papers are the need not only of using sulfanilamide but of attacking the foci of infection and, second, the advisability not only of removing the foci of infection but occasionally of using the sulfanilamide whenever one anticipates the danger of meningitis.

In January 1937, a man was admitted to the hospital in whose case a diagnosis of neoplasm of the left temporal lobe was made. There was no reason to suspect an abscess in this case. At operation Dr. Groff observed an encapsulated abscess, which ruptured. Within twenty-four hours the laboratory reported a hemolytic streptococcus. I told the family that the patient would probably die in five days, but sulfanilamide was given and he made a good recovery. Since, I have seen several cases of what I call protective meningitis, which in earlier days would have resulted fatally. These patients recovered after the combined use of sulfanilamide and thorough eradication of the foci of infection.

DR. JOHN S. LOCKWOOD: In answer to the question whether the white matter was involved: I did not make sections of the entire brain but took sections only from the periphery. In closing I wish to raise the question whether one should put so much emphasis on the intrathecal administration of the drug. One should be cautious about putting much confidence in this route, because the organisms that really produce the invasive infection in hemolytic streptococcic meningitis are not on the surface, bathed by spinal fluid, but in the deeper layers. These invading organisms can be attacked by the drug acting through lymphatics and blood capillaries, but not through the spinal fluid. Moreover, the amount of drug which can be given intrathecally is trivial as compared with the total amount required to control invasive infection. Although one is at liberty to give sulfanilamide intrathecally, I do not think that much emphasis should be placed on that part of the therapy.

CASE OF PNEUMOCOCCUS TYPE III MENINGITIS, WITH RECOVERY. DRS. D. SILVERMAN and MELVIN W. THORNER.

A case of meningitis due to a type III pneumococcus in a Negress aged 47 is reported. The source of the infection was in the left mastoid. Type III pneumococci were found in pus from the ear and in the spinal fluid. The patient was too ill for any surgical procedure. Complicating conditions were marked hypertension, moderately severe diabetes mellitus and a history of chronic alcoholism. Treatment consisted of administration of sulfanilamide by mouth. The patient recovered completely from the meningitis. She died of cerebral arterial disease four months after recovery from the meningitis.

DISCUSSION

DR. MELVIN W. THORNER: I always feel apologetic about presenting a single case, but this one seemed unique. Dr. Neal's series of cases did not, as far as I can see, include any instance of type III pneumococcus meningitis in which there was recovery, although in several cases meningitis of this type was treated with sulfanilamide. I believe that the present case, in which there was every reason to expect a fatal result, is strong evidence in favor of the fact that sulfanilamide should be used in treatment of meningeal infections of this type.

DR. J. C. YASKIN: This patient was under my care; I remember that she recovered, but I did not know that she had mastoiditis when my service terminated at the Philadelphia General Hospital last August. I have good reasons to believe that if I had known she had suppuration of the temporal bone and the diabetes was not too far advanced, I should have advised proper surgical intervention.

DR. B. J. ALPERS: One interesting feature in this case should be mentioned: There were a number of cells in the spinal fluid but no organisms. The brain was absolutely clean, according to the reports at autopsy. This indicated a meningeal reaction arising from the mastoid, which was apparently very active.

DR. MELVIN W. THORNER: The reason that mastoidectomy was not performed in the interval between the first and the second acute illness is that the patient was apparently recovering and showed no evidence of mastoiditis. During the second illness she presented a poor surgical risk, so that nothing was done.

LYMPHOCYTIC CHORIOMENINGITIS: REPORT OF A CASE, WITH AUTOPSY. DR. LAURENCE M. WEINBERGER (by invitation).

Within the past few years the clinical syndrome of so-called benign lymphocytic meningitis has become fairly well defined and usually recognizable. The discovery by Armstrong and by Rivers of a causative virus and a means of its identification by the neutralizing antibody reaction has in many cases allowed the disease to be differentiated from others presenting similar clinical features. However, from a pathologic point of view almost nothing is known concerning the disease in human beings.

Lillie and Findley, Alcock and Stern, in studies of the nervous system of common laboratory animals inoculated experimentally with the virus, observed a uniform pathologic picture. It was characterized by a lymphocytic meningeal inflammation and pronounced inflammatory and exudative changes in the choroid plexuses. In addition, variable amounts of ependymitis with ependymal desquamation and subependymal infiltrations were noted. The remaining parenchyma of the brain and spinal cord was normal.

In the case of lymphocytic meningitis occurring in man, reported by Viets and Warren, which, however, was not verified by virus studies, microscopic study revealed evidences of widespread encephalitis and inclusion bodies within ganglion cells. It is doubtful whether this was a genuine case. Barker and Ford reported the case of a woman whose condition was diagnosed as an acute meningeal episode and verified by identification studies of the virus as lymphocytic choriomeningitis. An operation was performed later because of developing paraplegia, and adhesive arachnoiditis of the spinal cord was observed. It appears, then, that marked meningeal thickening may follow the acute episode. Since there have been recorded no other verified cases in human beings in which pathologic studies were made, the following case is reported because the clinical picture of choriomeningitis was presented; the patient died, and a study of the brain revealed changes identical with those described in laboratory animals.

A boy aged 14 had experienced headache ten days before admission to the hospital, and complaints of photophobia, anorexia and weakness followed rapidly. Within a few days the patient had a number of shaking chills and vomited frequently; the neck became stiff.

On admission he was drowsy and lay in bed with the head hyperextended and the legs flexed; the temperature was 101 F. Except for congestion of the turbinate

bones, general examination gave essentially normal results. Neurologic examination revealed only pronounced meningeal signs. Serologic tests with the spinal fluid gave negative results, and no acid-fast organisms were found on repeated examinations.

Passage of the spinal fluid through a series of guinea pigs killed the animals; they showed no evidence of tuberculosis. Neither was there any instance of spontaneous encephalitis. No virus neutralization studies were made.

The boy gradually improved, and the degree of pleocytosis, which had risen as high as 900 cells, subsided on the eighteenth hospital day to 60 cells. On the twenty-eighth day of the illness, headache and nausea returned; the boy complained of violent vertigo, and a coarse nystagmus was noted. Lumbar puncture showed both cisternal and lumbar block. That afternoon he suddenly stopped breathing and could not be resuscitated.

Except for a few small patches of bronchopneumonia, general autopsy revealed nothing abnormal. The brain showed a marked foraminal ring constricting the cerebellar tonsils. The meninges were thick and of milky appearance. There was mild dilatation of the entire ventricular system. Tiny hemorrhages were seen under the ependyma.

Microscopically, there was marked thickening of the meninges, with obliteration of the subarachnoid channels by fibroblastic proliferations and lymphocytic infiltrations. This was most marked at the base and about the brain stem. The choroid plexuses were fragmented, denuded of epithelium and occupied by dense masses of inflammatory cells and exudates. The ependyma throughout the entire ventricular system was almost completely desquamated. A narrow subependymal zone was the site of numerous focal perivascular infiltrations and small hemorrhages. In this narrow zone there was an intense reactive gliosis, which at many points resulted in the formation of small ependymal granulations. The rest of the brain, studied with a variety of stains, was normal. There were no evidences of degeneration of ganglion cells, perivascular infiltrations, vascular changes or myelin disease.

From the coincidence of the lumbar and cisternal block with death and the observation of obliterative arachnoiditis and dilatation of the ventricles, it appears that death was due to intracranial hypertension. The pathologic changes in the brain appeared insufficient to cause death.

The pathologic changes were identical with those reported in animals, and while neutralization studies were not made, the death of several guinea pigs following injection of the patient's spinal fluid suggests the presence of virus.

Apparently, death may occur if the disease is sufficiently protracted for the development of adhesive arachnoiditis and intracranial hypertension. Evidently, under these circumstances the clinical term "benign" can hardly be retained.

### DISCUSSION

DR. F. H. LEWY: Two points in this presentation deserve discussion. The first bears on the examination of the spinal fluid. In this case, as in that of Viets and Warren, chlorides were considerably decreased in the spinal fluid, suggesting the possibility of tuberculous meningitis. However, this decrease was not absolute, but was relative to the protein content, because of the high prontosil values. In other words, a low chloride content of the spinal fluid has not the usual diagnostic value during treatment with prontosil. The second point is concerned with classification. During the last thirty years many investigators have expressed the belief that so-called benign meningitis is a clinical entity. Etiologic studies and controlled autopsy material have demonstrated that this assumption is wrong. In the first case reported by Viets, that of clinically typical benign meningitis, autopsy revealed meningoencephalitis, with marked involvement of the midbrain. Inclusion bodies were present, in contrast to the observations in animal experiments. A positive neutralization reaction has been described with the serum of persons who never had meningitis, whereas it has failed to appear in patients after the disease. The tests, therefore, do not indicate a uniform etiology. For the time being, the

collection of autopsy material seems to be the best method of controlling the clinical diagnosis of choriomeningitis.

DR. B. J. ALPERS: There is danger in assuming that in all cases the disease is caused by one virus or one factor. It is known clinically that in many cases the virus found by Rivers and Armstrong and Lillie is not neutralized. It is a mistake to say in all cases the disease is due to the same virus and should always show the same features pathologically.

DR. LAWRENCE M. WEINBERGER: I agree fully with Dr. Lewy. However, it seems that with so much uncertainty regarding the specificity of the virus-neutralizing antibody reaction, clinicopathologic correlations furnish the best means of establishing the entity of this disease, if it is an entity. Fortunately or unfortunately, the dearth of cases in which there was fatal termination precludes the accumulation of much pathologic knowledge, and apparently a long time must elapse before an adequate number of cases will have been studied. From a study of this case I am tempted to conclude that probably the same pathologic localizations occur in man as in monkeys after experimental inoculation.

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## PHILADELPHIA PSYCHIATRIC SOCIETY

BALDWIN L. KEYES, M.D., *President, in the Chair*

*Regular Meeting, Nov. 11, 1938*

ANOREXIA NERVOSA AS A MANIFESTATION OF COMPULSION NEUROSIS: A STUDY OF PSYCHOGENIC FACTORS. DR. HAROLD D. PALMER and MAXWELL S. JONES, M.B., M.R.C.P. (Edin.), London (by invitation).

We present 4 cases in which almost all the clinical and laboratory features of Simmonds' pituitary cachexia were present, but which on close examination of psychopathologic factors emerged as instances of severe neuroses. The clinical diagnostic term "anorexia nervosa" could be applied more or less appropriately to the disturbance in this group of cases, but we cannot, in the light of our demonstration of a classic compulsion neurosis personality in all cases, utilize the term "anorexia nervosa" as anything but a point of departure for our discussion. Recently the medical literature has shown a trend in the direction of differentiation between Simmonds' disease (pituitary cachexia) of a progressive fatal type and a more benign "functional pituitary cachexia." There is support for the view of some authors that "anorexia nervosa" is a form of the so-called functional pituitary cachexia. Scant reference can be discovered to the emotional factors which are readily found in all cases of "anorexia nervosa," and only a few recent articles have presented even brief descriptions of the personalities of the patients, otherwise completely studied and discussed.

In our 4 cases there were the following common denominators: In the physical sphere: (1) marked emaciation, the weight at the time of admission averaging only 77 pounds (39.4 Kg.); (2) hypothermia; (3) hypotension; (4) premature aging; (5) marked dehydration; (6) scant pubic and axillary hair; (7) marked and unremitting anorexia with vomiting if food was forced; (8) remarkable and strikingly disproportionate abundance of physical energy, and (9) amenorrhea. In the laboratory findings: (1) low basal metabolic rate; (2) disturbance of carbohydrate metabolism, as shown by dextrose and insulin tolerance tests; (3) normal hematologic and blood chemical constituents; (4) normal roentgenographic findings in the gastrointestinal studies, and (5) no evidence of pituitary disease demonstrable by roentgenography. In the psychic sphere: (1) unhappy home relations, with spoiling and overindulgence on the part of one parent and hate and hostility directed toward the other; (2) distinctly introverted personality type; (3) intellectual superiority; (4) marked, unmitigated stubbornness; (5)

temper tantrums; (6) impulsive outbursts; (7) meticulous, deliberate and obsessive mental habits; (8) excessive orderliness; (9) frustration in heterosexual adjustments; (10) ambivalence and compulsiveness, and (11) characterization by the family as "strong minded, stubborn, determined, of high ideals, not amenable to reason, self willed, evasive, overly sensitive."

It seems to us that a cardinal feature in all cases was the poorly adjusted personality. There were many regressive, infantile reactions, much spoiling and the desire to dominate in a restricted environment, together with intolerance of frustration, ambivalence, selfishness and stubbornness. In addition, the history furnished by the family indicated headstrong idealism and many perfectionistic traits. This constellation of reactions is the basic neurotic personality of "anorexia nervosa." This series of terms sums up the basic personality of compulsion neurosis. The second cardinal feature of the 4 cases was the appearance of the illness in each instance as the result of some emotional conflict or trauma. The inability to face and solve the conflict resulted in regression. A third feature was the biphasic nature of this symptom, in which two purposes were clearly visible: (1) the intense repression of hostile instinctual impulses in which the self-punitive and expiatory symptoms dominated, and (2) an element of gratification. Another interesting feature was the presence of insight. There was a mixture of strange, contradictory impulses and behavior, on the one hand, and intellectual acuity, even superiority with partial insight, on the other. The patient professed to have no faith or belief whatever in the fears arising from internal sources, but nevertheless adhered to them desperately.

Treatment in all the cases was successful and consisted only of superficial psychotherapy, with an indirect attack on the total maladjustment of the personality. All efforts at coercion, exhortation, persuasion and coaxing were strictly avoided. In fact, throughout the treatment little reference was made to anorexia or vomiting, nor were there any diet lists, frequent weighings or other regimen of that kind. The family was requested to cooperate in the avoidance of reference to these aspects of the problem. The poor prognosis for "anorexia nervosa" may often result from failure to recognize the compulsive nature of the disorder. Compulsion neurosis is of profound depth and cannot be dealt with by a frontal attack.

*Summary.*—We believe that the term "anorexia nervosa" should give way to the more inclusive and accurate psychiatric title compulsion neurosis. "Anorexia nervosa" is really the term applied to a compulsion neurosis the pattern of which is fixed on anorexia and vomiting, together with the resulting emaciation, only after the condition has reached an advanced state and has become more or less an irreversible pattern. "Anorexia nervosa" really belongs in the same category with "gastric neurosis," "sexual neurosis" and "puerperal psychosis," which are now psychiatrically obsolete.

DISCUSSION

DR. J. C. YASKIN: Any presentation that helps in the treatment of the patient is worth while, and there can be no question that the report of Dr. Palmer and Dr. Jones has therapeutic value and many other interesting features.

I have never seen a case of anorexia nervosa—at least, until this evening I did not think I had seen any. After hearing the paper, I have not a doubt that I have seen a great many cases in which the conditions came under this classification. I never called them that. To me they were forms of psychoneurosis or psychosis in which anorexia and malnutrition were profound manifestations.

I believe that the compulsive type of reaction is not the only one accompanied by such symptoms as the loss of appetite. Some depressive reactions are commonly accompanied by loss of weight and appetite, and some neurasthenic reactions show the same tendency, though not as marked, perhaps, as Dr. Palmer's cases indicate.

I was much interested in the approach used in defining the personality of the patient before the development of the illness, which, as delineated, is the type that all recognize in compulsive neurosis.

I am at a loss to understand, and I hope Dr. Palmer will elucidate, the recovery that took place in the third case, the patient who went home against the wishes of the physicians at the hospital and gained a number of pounds shortly thereafter. Was the condition a psychoneurosis, or something else? One often sees patients with depressive types of reactions who do exactly that, especially those with the mild depressions which do not show up clearly.

DR. HAROLD D. PALMER: Undoubtedly, all see many patients with the compulsion neurosis and gastrointestinal symptoms, who possibly are starting on the way to emaciation, debility and even death. In other words, it may be that the condition in these cases could be described as early "anorexia nervosa." The tendency in the literature is to regard hysterical anorexia, obsessions about food and the general neurotic, "picky" appetite as neuroses *per se;* then, when the pattern of anorexia becomes fixed, the emaciation marked and the whole process more or less irreversible, the label "anorexia nervosa" is applied. I am interested in Dr. Yaskin's remarks about the similarity of the condition to schizophrenia in some cases. The mention of the resemblance to schizophrenia is particularly interesting in case 2 which I cited, that of a girl who in college showed an episode of strongly schizoid character in which ideas of depersonalization predominated. I think it possible that any one who had seen her at that time would have labeled the case as one of early schizophrenic process. I am sure all have seen the state of frozen panic which occurs in compulsion neurosis, in which the ambivalence reaches a point of absolute inactivity which might be called a catatonic state. I think it was Fenichel, in his "Outlines of Clinical Psychoanalysis," who called advanced types of compulsion neurosis terminal states forming a transition to schizophrenia. He tended to regard them as irreversible reactions. In Abraham's table of the development of the libido, quoted extensively by Fenichel, the compulsion neuroses rank considerably above paranoia and paranoid reactions, the manic-depressive personality and schizophrenia. Certainly, they should be included in the ambivalent states with hysteria and not in the preambivalent states of complete autoeroticism or schizophrenia. I recall a patient with a severe compulsion neurosis who was so fixed in his ambivalence that he would stand in the middle of the floor for hours, unable to move, unable to eat and so completely bound that he could not get to the bathroom to attend to body processes. That state of absolute ambivalence often resulted in distention of the bladder, and not uncommonly the patient soiled himself. Any objective evaluation of this state would certainly result in classification as an irreversible terminal state of compulsion neurosis. However, this man was given the narcosis treatment, recovered to a certain degree of social adjustment, spent six months in Germany and Austria after the treatment and is now able to earn part of his living in a competitive business. Of course, another resemblance between compulsion neurosis and schizophrenia is the richness of symbolism evident throughout the symptomatology. I think it was Steckel who said: "Symbolism is the tyrant of the compulsion neurotic."

In reply to Dr. Yaskin's question about the recovery in case 3, I should enlarge on the clinical psychiatric findings to clear up any confusion which might appear to exist regarding the presence of depression. There was no self accusation, mental retardation, physical inertia or despondency. The patient's statement: "Everything is dead, and I am disillusioned. The world no longer has any meaning," referred to her marital life. It seems to me that this reaction is to be differentiated from that of the depressive person who believes that the origin of his suffering is within. In this case the mechanism was one of projection; that is, "The outer world has done this to me, or it has been done to me and not by me." I may say that the patient recovered after removal from the environment, which obviously represented constant emotional tension and stress.

The really significant point which we wished to bring out in the presentation of the 4 cases is that when studied from a psychiatric point of view "anorexia nervosa" yields an enormous mass of psychopathologic material and psychically determined symptoms, which fall most appropriately into the classification of compulsion neurosis.

AUDITORY AND FORMED VISUAL HALLUCINATIONS IN A CASE OF MENINGIOMA OF THE BRAIN. DRS. TEMPLE FAY and MICHAEL SCOTT.

A woman aged 45 for a period of three years had complained of monthly convulsions on the right side and unconsciousness, often preceded by an aura of "giddiness" and numbness in the right arm and leg. Occasionally there occurred an aura of fortification spectrums, without definite visual loss, more marked on the right side. Gradually she complained of persistent noises in the vertex, described as "crickets." Two and a half years after the initial complaint she began to experience diurnal combined visual and auditory hallucinations of groups of people or "quartets." She could see only the upper half of these persons, and they appeared to her singing church hymns or "Uncle Ezra Barn Dance Songs." The figures described by the patient wore apparel of various vague colors. She could never accurately identify these persons, but the pitch of the voices suggested that they were female.

Coincident periods of jargon aphasia, anomia and verbigeration occurred, during which her husband feared she was "going crazy." At times the visual hallucinations preceded the convulsion by a few hours or days.

Neurologic examination revealed dulness over the left parietal boss on percussion, right homonymous hemianopia and slight hemiparesis with hyperreflexia on the right, but clonus and the Babinski and Hoffmann signs were not elicited. There were hypalgesia and hypthermesthesia over the entire right side of the body. Slight atrophy of the muscles of the right hand was detectable, but there was no astereognosis or disturbance of position sense. The patient was predominantly right handed.

Roentgenograms showed a shift of the pineal gland to the right. A preoperative diagnosis was made of cerebral tumor on the left involving the temporo-occipital area.

Exploratory craniotomy disclosed a tumor on the mesial surface of the left superior parietal gyrus. The tumor, 7 cm. in diameter, was well encapsulated and had its origin from the falx, just above the reflection of the tentorium. Compression of the paracentral lobule, anteriorly, and the precuneus, posterolaterally, was marked. The left lingual gyrus and the superior parietal gyrus had been displaced laterally.

Histologic studies established the diagnosis of meningioma.

Prompt recovery followed operation. The patient has remained free to date from the hallucinations formerly experienced.

The right upper quadrants of the visual fields have partially returned. The hemiparesis and hemihypalgesia have disappeared, and there have been no convulsive seizures.

Postoperative tests for optokinetic nystagmus revealed a normal number of movements to either side and bilateral preservation of the centrifugal optomotor tracts (Spiegel).

DISCUSSION

DR. H. D. PALMER: I have little to add to this demonstration of skilful neurosurgery and to the interesting discourse on organic hallucinations. I wish, however, to ask Dr. Fay how much suggestion there was in arriving at the specific nature of the hallucinations in this case. I ask the question because Horrax has carefully differentiated types of organic hallucinations. Several years ago Harrow, Schwarz and I reported an interesting case.

A girl aged 14 had a cyst in the occipital bone which intruded into the interior of the skull and compressed the right occipital pole. The hallucinations described by the patient resembled vague, cloudlike objects moving across the field of vision or clouds in the periphery of the visual fields. At times the patient stated that they were like something moving past her door. By suggestion, however, I was able to get her to describe a specific hallucination which, unquestionably, had its origin in a vague, unsystematized and undifferentiated visual impression. She said: "It is my mother's bier. My mother is dead." The important thing is that, as the result of psychopathologic motivation and suggestion, this organic hallu-

cination of vague character became a specific visual impression of her mother's corpse being wheeled past the door on its bier. In attempting to understand the basis of this interpretation by the patient it was necessary to look into her early background; there it was found that she had frequently been beaten in childhood, had a great deal of hostility, antagonism and jealousy toward her mother and had often wished the mother dead. It seems to me that one can say in general that an organic hallucination is one of undifferentiated character, but the specific direction which these vague hallucinations take is determined by the psychopathologic background of the patient.

DR. TEMPLE FAY: What Dr. Palmer said about delineation of the hallucinations is true. The organic type is ill defined.

OBSERVATIONS ON THE ELECTROCARDIOGRAPHIC PICTURE DURING METRAZOL THERAPY. DR. JAMES A. FLAHERTY, DR. HOWARD P. ROME (by invitation) and WILLIAM ZINTL (by invitation).

We present a preliminary report of work now in progress in the department of mental and nervous diseases of the Pennsylvania Hospital concerning the electrocardiographic picture during the course of metrazol therapy of psychotic states. Electrocardiograms were arbitrarily taken at irregular periods in relation to the time of the convulsion but in sequence in each successive group of five such treatments. The purpose was to detect, if present, evidences of induced cardiac changes in otherwise healthy persons as an untoward effect of shock therapy.

Other investigators (Orenstein and Himwich) have hinted at the possibility of cardiac pathologic changes incident to the induced state of anoxemia. The permanence of well recognized electrocardiographic abnormalities in anoxic states has been the subject of fairly extensive investigation. Kountz and Hammouda, Rothschild and Kissin, Katz and his associates and others have reported extensively on the typical tracing in such conditions. All mentioned the evidence of danger of low oxygen tensions in potential cardiac pathologic states, in contradistinction to the relatively innocuous aberration seen in normal persons.

Because of the widespread use of the new convulsive therapies of the psychoses and the recognized sizable incidence of potential and existent heart disease in any cross section of the population, it was believed that a better evaluation of the therapeutic morbidity was in order. This is indicated in view of the more recent use of metrazol in treatment of persons in the older age group, viz., those with involutional psychosis, particularly since there has not been a sufficient interval of observation of untoward effects of this therapy in any group of cases reported to date.

Pretreatment tracings in each case were wholly within normal limits. The following relations were considered—changes correlated with the time since the last treatment, occurrence of convulsion or psychic equivalent and dose of the drug.

Such changes as were observed simulate those seen in experimentally and naturally occurring states of anoxia: (1) progressive flattening to the point of inversion of the T wave; (2) changes in the level of the ST segment; (3) changes in the basic cardiac rate; (4) prolongation of the time of electrical systole; (5) accentuation and initiation of rhythm disorders—premature contractions—tachycardia and bradycardia; (6) progressive diminution of the amplitude of the entire complex. The picture simulates that seen with insufficiency of the coronary arteries, either intrinsic, incident to local pathologic conditions, or induced, incident to systemic anoxemia.

Binet and other French investigators have demonstrated experimentally the sequence of a progression of such changes in the presence of progressive diminution of environmental oxygen tensions. These changes are reversible, whether the deficiency is one of environmental oxygen lack primarily or of oxygen deprivation incident to carbon monoxide poisoning or dependent on ischemia, if normal conditions supervene before irremediable myocardial changes occur.

For these reasons, our tracings have been taken usually no sooner than from four to six hours after treatment, in an effort to establish a ratio for recovery

time. In some cases, in which tracings have been taken at intervals of two weeks for as long as three months after the last treatment, slight changes are still apparent.

Realizing the incomplete state of our data and the fallacy of inferential reasoning, we offer these tentative conclusions: (1) Metrazol therapy of mental disease is not without cardiac side effects which have an as yet unevaluated permanence; (2) such effects are comparable with those seen electrocardiographically in disease of the coronary arteries; (3) as a corollary, anoxemia is the etiologic factor; whether such insufficiency is local, systemic or medicamentary awaits a longer period of observation; (4) with the high incidence of recognized and potential heart disease in any cross section of the population established historically, clinically or, more accurately, electrocardiographically, the use of metrazol imposes an as yet unevaluated cardiovascular risk. The latter is in direct ascending ratio to the age of the patient.

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## BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

TRACY J. PUTNAM, M.D., *Presiding*

*Regular Meeting, Nov. 17, 1938*

CLINICAL AND ANATOMIC STUDIES IN MONGOLISM. DR. CLEMENS E. BENDA.

The so-called mongoloid deficiency is characterized by a combination of mental deficiency and physical stigmas, such as slanting eyes with epicanthal folds, depressed nose, flattening of the face, high cephalic index, short broad hands, short feet with a deep gap between the big toe and the second toe, and fissuring of the skin. The amazing fact in regard to mongolism is the resemblance of one mongoloid child to others of the same type. How does it come about that these children have such similar faces and are so much alike that most of them could be regarded as brothers and sisters? Other constitutional defects do not obliterate the individual differences due to race and family, even when deterioration has completely replaced all expression of individuality. This fact has given rise to a number of speculations in which mongolism is regarded either as a germ mutation or as an atavistic regression, as Crookshank stated (The Mongol in Our Midst: A Study of Man and His Three Faces, ed. 3, London, George Routledge & Sons, Ltd., and Kegan Paul, Trench, Trubner & Co., Ltd., 1931). However, in spite of the amazing resemblance, a more detailed study of mongoloid children reveals that no one of the features usually mentioned is essential and will establish the diagnosis with undisputed certainty. Hence many authors have offered tables of the various characteristics which may be present in a number of cases, and Tredgold (Stewart, R. M.: Problem of the Mongol, *Proc. Roy. Soc. Med.* [*Sect. Psychiat.*] **19**:11 [March] 1926) denied that mongolism is a clinical entity.

It was my aim in this research to determine the essential character of the mongoloid monstrosity, since a satisfactory analysis of the physical appearance alone will enable one to discover the essential disorder. In a study of more than 150 mongoloid patients, exact measurements of the skull and a study of the growth have made it clear that there is a definite relation between mongolism and a peculiar formation of the skull which is more decisive than any other symptom.

A chart comparing the development of the normal and the mongoloid skull reveals that the curve of normal growth shows a great increase in size during the first year of life. The normal skull gains more than 10 cm. in circumference during the first twelve months of life. After that, the curve rises more slowly. The curve for the mongoloid skull is much less steep and reaches a point at the age of 9 years which should be attained normally at the end of the first year. Practically no mongoloid skull exceeds 50 cm. (20 inches) in circumference.

Even more informative is an analysis of the development of the length and width of the skull, respectively. The length of the skull of a normal child increases rapidly during the first year of life; the gain is about 4 cm. The mongoloid skull fails to increase, especially in length; the length after the first year does not correspond with even that of a normal child of 6 months, and the length of the skull of a normal child aged 1 year is reached by that of the mongoloid child at the age of 8 years. The skull of an adult with mongolism is not larger than that of a normal child aged 3. Another point, worthy of even more emphasis, is that failure in growth of the mongoloid skull is most marked during the first months of life. After the third year, the curves are approximately parallel, but the growth of the mongoloid skull does not compensate for the failure during the first months after birth.

The curve for increase in width of a normal and that for a mongoloid skull correspond more closely; though the mongoloid skull is strikingly brachycephalic, its width never exceeds the normal. It should be noted that the mongoloid skull at birth does not differ from the normal in measurements.

What enables the skull of a normal child to increase so markedly during the first months of life? The increase is due only partly to true growth of tissue. Of more importance are the turns of the skull base. The squama of the occipital bone moves downward and protrudes horizontally. The clivus and the anterior cavity become flattened; in later years the development of the sinal system is an important factor in molding and increasing the size of the skull. These changes in the skull, especially the base, which have been known since the studies of Virchow, are accompanied by proliferative growth of cartilage and bone. The mongoloid skull is deficient in proliferative growth and lacks all the turns previously mentioned. As a fact, the mongoloid skull maintains the embryonic features characteristic of the last months of intrauterine life and carries this outline into the later stages of development.

Autopsies in 11 cases furnished sufficient evidence that the mongoloid skull presents a definite shape, which may be characterized briefly as follows: The occipital squama was extremely steep and continued rather in the direction of the cervical spine, which was more upright than in normal children. The condyles of the occipital bone were underdeveloped; the foramen magnum was greater in the oblique than in the sagittal diameter; the sphenoid bone was extremely small. In no case did I observe a sphenoid sinus, which can be expected at the age of 7 years. This fact was checked by more than 20 roentgenograms. The cribriform plate was small and retracted; the frontal bone was flattened and free from the molding which is characteristic of the forehead of man. The lack of development of the face was also striking.

Autopsies revealed also that the cartilaginous spaces were small and early ossified. Proliferation of the bony tissue was poor. This explains the fact that the fontanels in mongoloid children remain open for a long time.

The following roentgenographic data may be mentioned: A lateral view of the skull showed a steep occipital squama, which is characteristic of mongolism but is by no means restricted to this condition. The sphenoid bone was extremely small, and the sella was sometimes more upright than in normal children. More striking was the anterior cavity, which sloped upward and outward. The roof of the orbit was protruding; the cribriform bone appeared short and retracted; the nasal bone was also retracted. Besides the lack of a sphenoid sinus, there was definite lack of development of the frontal sinus. In only 2 cases in my material was there a suggestion of a frontal sinus, and in both instances many deviations made the diagnosis of mongolism doubtful.

In a posteroanterior view the most striking feature was the slanting of the orbital holes. The upper margin of the orbit sloped upward and outward, and in some cases the orbital cavities were egg shaped. The lack of a frontal sinus was readily recognizable in this view.

In 1 case, when the patient was seen first at the age of 11 days, the diagnosis was doubtful because of the epicanthal folds and slanting of the palpebral fissures.

A lateral roentgenogram revealed a large body of the sphenoid bone and a distinct cartilaginous space between the occipital and the sphenoid bone. On the basis of this finding, the diagnosis of mongolism was ruled out. I had the opportunity to observe this child during the next year, at the end of which there was slight hydrocephalus and the diagnosis of mongolism could be abandoned.

Anatomic studies have resulted in the accumulation of evidence that the so-called mongoloid features represent a pathologic entity which can be attributed entirely to a deficiency of growth and development and which has not the slightest relation to the Mongolian race. The resemblances between mongoloid children are due to a special type of skull formation. However, the mongoloid deficiency is not restricted to the development of bone; all ectodermal derivatives—the skin;

*The Pituitary Body in Patients With Mongolism*

| No. | Age | Sex | Weight, Gm. | Acidophils | Chromophobic Cells | Basophils |
|---|---|---|---|---|---|---|
| 1 | 2 days | F | .... | Increased in number | Poor; pyknotic | Absent |
| 2 | 6 wk. | F | .... | Absent | Predominant | Few present; amphoterous |
| 3 | 3 mo. | M | .... | Absent | Predominant | Few present; amphoterous |
| 4 | 5 mo. | M | 0.085 | Predominant | Present in small numbers | Absent |
| 5 | 6 mo. | F | .... | Predominant | Present in small numbers | Absent |
| 6 | 7 mo. | F | 0.1 | Predominant | Few present; small | Absent |
| 7 | 7 mo. | M | 0.065 | Predominant | Small; abundant | Absent |
| 8 | 8 mo. | M | 0.22 | Well developed; conspicuous | Small | Absent |
| 9 | 13 mo. | M | .... | Numerous | Numerous | Absent |
| 10 | 18 mo. | F | .... | Predominant | Small; abundant | Absent |
| 11 | 8 8/12 yr. | M | 0.7 | Present | Numerous | Forming acini; "signet cells" |
| 12 | 9 8/12 yr. | F | 0.3 | Predominant in lateral fields | Present in middle field | Few present in middle field |
| 13 | 10 yr. | F | 1.1 | Predominant | Present | Few; immature |
| 14 | 12 yr. | F | 0.3 | Predominant | Present | Few in middle field |
| 15 | 14 5/12 yr. | M | 0.6 | Present | | Postmortem changes |
| 16 | 20 6/12 yr. | M | 0.8 | Predominant | Few | Few in middle field; "castration cells" |
| 17 | 30 8/12 yr. | M | 0.9 | Abundant | Few | Absent |

the epithelial glands; the epithelial linings of the oral and nasal cavities; the conjunctiva, and, last but not least, the nervous system—are involved.

In the following paragraphs, I shall present the pathologic changes in the pituitary body which I believe are of most interest. The table represents a survey of 17 cases. A detailed description of 13 of these cases will appear in a future issue of the ARCHIVES. Therefore, I may offer here merely a few explanations which appear useful in establishing the theories under consideration.

It may be mentioned that a sex difference in the distribution of cells could not be noticed. The 17 cases may be divided into four groups: 1. In 7 cases (nos. 4, 5, 6, 9, 10, 13 and 17) no basophils were observed. The cells were present as a densely piled conglomeration of rather round cells, most of which had a distinct eosinophilic protoplasm while some had not. However, the chromophobic cells which were present may properly be regarded as juvenile eosinophils. In case 17 the arrangement of the cells was columnar and gave the impression of pathologic growth. 2. In 2 cases (nos. 2 and 3) the anterior lobe was almost entirely com-

posed of densely piled chromophobic cells without differentiation. Few basophils were recognizable; they stained blue with the Mallory stain, but showed amphoterous reactions to other methods. 3. In 3 cases (nos. 1, 7 and 8) many eosinophils were present; however, the chromophobic cells covered larger areas. They were small, and most of them showed degenerated nuclei. In some areas the protoplasm stained violet and blue without distinction. These cells may belong to the basophilic system, or they may not.

In these 12 cases the pathologic picture was conspicuous. In group 1 there was marked increase in eosinophils, which predominated, while the basophils were absent. In group 2 the embryonic chromophobic cells prevailed and were not differentiated, except for a few amphoterous cells. In group 3 the degeneration of the chromophobic cells was remarkable, while eosinophils were not conspicuous. All three groups were similar in that there was a definite failure in the development of the chromophobic and particularly of the basophilic cells.

There were 4 remaining cases (nos. 11, 12, 14 and 16), of patients aged 8, 9, 12 and 20 years, respectively, in which the pituitary did not show pathologic changes at first sight. In these cases, except no. 11, there was an increase in eosinophils, which covered the lateral fields of the gland in horizontal sections. They were densely piled, and these areas did not show chromophobic cells or basophils. In case 11 piling up of the eosinophils was also obvious in many sections. However, this observation was not as distinct. In the other 3 cases there was marked difference between the lateral fields and the trigonum Rogowitsch. The latter showed small chromophobic and small basophilic cells of the type which is usually seen in the pars intermedia. These types of cells prevailed exclusively, and there was little invasion of the eosinophilic areas. In case 11 the basophils were conspicuous and formed whole acini in some cases. Although in these 4 cases the pituitary appeared altered as compared with the normal gland—castration and signet cells were easily recognizable—the pathologic picture was not typical. It seems to me that these observations may be considered as indicative of regeneration in which the endocrine system had established equilibrium. It may be kept in mind that these cases were instances in which there was a hyperactive, even goitrous, thyroid; it is suggested that the activity of the thyroid influenced the histologic picture of the pituitary.

The interpretation of these observations may still be a matter for discussion, since it is impossible to decide whether premature increase in eosinophilic cells or failure in development of the basophilic system is of more importance. Personally, I am inclined to emphasize the significance of the latter. The increase in eosinophilic cells may be compensatory or due merely to the lack of basophilic and chromophobic cells. There are many indications that hypopituitarism of a special type is the main cause of mongoloid deficiency. Regardless of these questions, I feel safe in stating that the clinical investigations have revealed sufficient evidence that mongolism represents a congenital hypopituitarism that is still present and effective in the first years of life. Confrontation of the clinical features of acromegaly and mongolism reveals that the situation in the two conditions is reversed. One must keep in mind that in all endocrine disorders the time factor is of decisive importance in its influence on the clinical picture.

My pathologic studies have verified the clinical conclusions and furnished sufficient evidence that in cases of mongolism a disorder of the pituitary is invariably present. Mongolism appears as congenital dyspituitarism or hypopituitarism, as cretinism has proved to be congenital hypothyroidism.

DISCUSSION

DR. R. K. BYERS: Mongolism is a uniform syndrome. What has always impressed me is that the syndrome is present completely or not at all.

DR. H. HALE POWERS, Wellesley, Mass.: It used to be said that mongolism is most likely to occur in the youngest child of a large family, and the condition

was by some supposed to be related to exhaustion of the child-bearing functions of the mother. Is that still taken seriously?

DR. TRACY J. PUTNAM: My own experiences with the hypophysis have led me to feel fairly certain that it is eosinophilic cells in the anterior lobe which are the carriers of the growth principles. On the other hand, destruction of the hypophysis has only a distant similarity to mongolism, and it is astonishing how little mental and intellectual functions are impaired when there is damage to the hypophysis. I wonder if Dr. Benda has any explanation of the fact that the result of marked increase of eosinophils is perverted growth and mental deficiency.

DR. C. E. BENDA: The age of the mother is still a point of much discussion. My charts show that 6 per cent of the mothers were from 15 to 20 years of age; 9 per cent, from 21 to 25; 19 per cent, from 26 to 30; 25 per cent, from 31 to 35; 20 per cent, from 36 to 40, and 15 per cent, from 41 to 45. Sixty per cent were over 30. On the other hand, there was an equal number below the age of 35. The chart shows definitely that age is of some importance, but it is not the essential factor.

The question is whether there is any relation between the maternal age and the pathologic condition of the pituitary that I demonstrated. It is known that in pregnancy the maternal pituitary suffers enlargement. The usual cell composition is changed; the eosinophils are increased in number. There is a high tax on the function of the pituitary during pregnancy. It seems to me that the most acceptable explanation of the relation between the maternal age and the pathologic condition of the pituitary associated with mongolism is that the maternal pituitary in the older groups is not likely to adjust itself to the condition of pregnancy. Thus, temporary deficiency arises. This, however, is still speculative.

In answer to Dr. Putnam's question: It is true that the known diseases of the pituitary are usually not associated with mental impairment. However, these conditions occur after the development of the brain is completed.

There are two lines of animal experimentation of interest to the mongoloid condition. Experiments with feeding thyroid substance have shown that excess of thyroid causes early differentiation followed by dwarfism and a peculiar shape of the head. The same effect can be obtained through pituitarectomy early in life. However, most of the experiments with pituitarectomy have been made on dogs at the age of several months. Aschner claimed to be the only man who succeeded in removing the pituitary in very young dogs. He observed dwarfism, a peculiar shape of the head and mental impairment.

I am conscious that the high number of eosinophils in the pituitary of mongoloid children is difficult to explain. I do not know which is of more importance, the increase in eosinophils or the deficiency in basophils. If the former is to be emphasized, the time factor may be of decisive importance, and the increase of eosinophils may lead to early stimulation of the thyroid, with its sequelae. Personally, I am under the impression that the deficiency of basophils may be of more importance for an explanation of the mongoloid deficiency.

CLINICAL AND THEORETIC ASPECTS OF LESIONS OF THE FRONTAL LOBES. DR. KURT GOLDSTEIN.

In cases of lesions of the frontal lobe there are to be distinguished phenomena of sudden appearance and permanent symptoms (Goldstein, K.: Die Functionen des Stirnhirnes und ihre Bedeutung für die Diagnose der Stirnerkrankungen, *Med. Klin.* **19**:965; 1006, 1923).

*Sudden Attacks* (tonic character, in contrast to the clonic type characteristic of disease of the motor area).

1. Turning of head and eyes to the side opposite the lesion (area 8, frontal convolution II) (combined with extension and abduction of the contralateral arm and leg).
2. Turning and tilting of the body to the opposite side.
3. Subjective feeling of such turning without real movements.

4. Sudden sinking produced through contracture of flexor muscles (area 6).
5. Sudden sinking produced through loss of general tonus.

*Permanent Symptoms.*

*A.* Disturbances of maintenance of equilibrium.

I. Phenomena concerned with the body.

1. Abnormal postures (deviation directed toward the opposite side) of the entire body or parts of the body (premotor area, frontal I and II).
2. Involuntary movements as expression of the exaggerated tendency toward "preferred position" (deviation movements of the body, arm and hand).
3. Abnormal hyperreactivity to tactile stimuli on the "opposite" side.
   (*a*) Abnormal general startle on sudden stimulation.
   (*b*) Hypersensitivity of the labyrinth.
   (*c*) Abnormal turning movements to the side of the stimulus, whatever sense organ may be stimulated.
      (*aa*) Abnormal deviation of the body, arms, etc., on stimulation of the labyrinth and eye.
      (*bb*) Abnormal postures as expression of the stronger effect on "the opposite side" during stimulation of the organism arising from the usual environment.
      (*cc*) Deviation of the outstretched arms, etc.
      (*dd*) Past pointing.
   (*d*) Changes in the sensory sphere: spatial displacements of perceived objects; disturbances in the estimation of weights.
   (*e*) Tonic grasping; tonic response of the foot.
4. Decreased tone, especially of extensor muscles; increased innervation of flexor muscles (disturbance in standing).
5. Exaggeration of some associated movements.
   (*a*) Increase of the neck reflexes and similar phenomena.
   (*b*) The so-called Léri phenomenon (increase of tone in the flexor muscles of the forearm in passive flexion of the fingers and hand).
   (*c*) Increase of the Mayer phenomenon (increased opposition and adduction of the thumb in passive flexion of the second or third finger).

II. Phenomena concerned with the eyes and head.

(*a*) Impairment of voluntary movements to the opposite side.
(*b*) Deviation of the eyes to the homolateral side (secondary to the impairment described in *a*).
(*c*) Fixation nystagmus (in voluntary movements to the opposite side).
(*d*) Diminution of optokinetic nystagmus in the direction opposite the lesion.
(*e*) Apractic disturbance of ocular movements.

III. Disturbance of coordination of the body, head and legs in sitting, walking, standing (especially in bilateral lesions).

Disturbances included under headings *A* I, II and III together produce frontal ataxia.

*B.* Aphasia, apraxia, agraphia, amimia (lesions in the posterior part of frontal II and III).
Hypokinesis and akinesis (usually acute lesions of both frontal lobes).

*C.* Mental disturbances (impairment of the abstract attitude).
Lesions of the prefrontal region (Goldstein, K.: The Significance of the Frontal Lobes for Mental Performances, *J. Neurol. & Psychopath.* **17**:27, 1936).

The differences of opinion concerning the symptoms in cases of lesions of the frontal lobe are due to the inadequate attention which has been paid to the site, extent and nature of the lesion. Another factor lies in the differences in the manner of investigation. The various symptoms are developed more or less according to the localization of the lesion in the individual case.

However, the various symptoms do not represent phenomena which are only accidentally connected with the function of the frontal lobe. According to my concept, one is dealing with disturbances of performance which are similar in nature, the one in the bodily, the other in the mental, field. Just as the bodily "performance of direction" guarantees the turning of the organism toward a definite point, important with respect to the total situation, the psychic performance of the frontal lobe may be characterized as a mental guiding toward the essential of a total situation as a recognition and holding on to this essential and an emotional and wilful reaction to it. One might speak in this connection of a mental state of direction. With this view in mind, light is thrown on the spatial relations of the regions in the frontal lobes which are of significance for the positions of the head and eyes, erect carriage, speaking and writing. From the combination of these various functions specifically human behavior results. Thus, the concept outlined here furnishes the foundation for reaching an understanding of the specific role of the frontal lobe in the animal kingdom and its special development in man.

DISCUSSION

DR. DAVID M. RIOCH: It is interesting that Dr. Goldstein has been able to devise tests for human beings which do not involve the use of language. His results have been confirmed in monkeys by the work of Jacobson (*A. Research Nerv. & Ment. Dis., Proc.* **13**:225, 1932; *Comparative Psychology Monographs,* 1936, vol. 13, p. 3). The experiments of Richter and Hines (*Brain* **61**:1, 1938) suggest that the striatum plays a role in conjunction with the cortex in this behavior.

DR. TRACY J. PUTNAM: I should be grateful if Dr. Goldstein would speak of the relation between the forced grasping seen with lesions of the frontal lobe and the pseudoforced grasping sometimes seen in patients in coma without evidence of focal disturbance.

DR. KURT GOLDSTEIN: I find similar changes in behavior in patients with lesions of the frontal lobe and in those with diffuse lesions of the cerebral cortex. In most of the latter I think that, whatever the kind of impairment, there is dysfunctioning of the frontal lobe, and thus symptoms referable to the frontal lobe come especially into the foreground, because the most complicated function will be impaired first. All the other functions of the cerebral cortex may be impaired, too, in cases of diffuse lesions, but not to such a high degree.

In regard to the question of grasping, I should say that there are different kinds of grasping. Here I mean especially tonic grasping. This is clearly connected with the premotor area. I found that this type of grasping has to do with lack of function of the frontal lobe.

There is great similarity between my findings and those in animals with excision of the frontal lobes; but there are also characteristic differences. I do not believe that higher animals are capable of abstract behavior. It is a property characteristic of human beings. This behavior has much to do with language. Animals do not have a language similar to that of man because the ability to think abstractly is a prerequisite for language, and animals have not this ability.

# Book Reviews

**The Pharmacological Shock Treatment of Schizophrenia.** By Dr. Manfred Sakel. Foreword by Prof. Otto Pötzl. Translated by Joseph Wortis, M.D. Nervous and Mental Disease Monograph Series no. 62. Price, $2.75. Pp. 136, with illustrations. New York: Nervous and Mental Disease Publishing Company, 1938.

A notice on the title page says that Sakel's book is an "enlarged version of a series of articles from the *Wiener medizinische Wochenschrift,* 1934-35." It is to be regretted that the version is merely enlarged, perhaps also improved, but not materially revised. A suitable revision might have removed what is a decided weakness of the monograph: undue theorizing and dogmatic statement of opinion. Clinical experience of the past five years has conclusively shown that no rigid rules can be formulated concerning the technical manipulation of the patient with hypoglycemia and that the physiologic basis of the insulin effect is shrouded in obscurity. Nevertheless, Sakel continues to announce that "shock" must be discontinued when the patient with catatonic excitement passes into a state of somnolence and when the catatonic stupor gives way to excitement. The reason for the magisterial instruction is what it was five years ago: "that portion of the mind which happens to be most active at the time" must be allowed to become "fixated." The "latent portion" rises to the surface and "achieves dominance over the former portion." The well known, but ill founded, hypothesis of the "neutralization of the excitant hormone and blockade of the nerve cell" is retained in the present enlarged version, and the high-sounding terms familiar from the 1934 publications —"vagotonic muffling of the cell," "polarization of pathways"—are repeated over and over again, although they are used "only figuratively." Apparently aware of the vagueness of his anatomicophysiologic speculations, Sakel attempts to buttress his "working hypothesis" with quotations from Hughlings Jackson, Stransky and Storch. But the support borrowed from the authors merely emphasizes the necessity for borrowing.

The many pages of fruitless speculation are merely a deplorable blemish in a book which otherwise offers excellent description of cases and technic and fairly teems with sound observation. Unfortunately, the value of the descriptive part of the treatise is also vitiated by the author's penchant for dogmatic statement. It is, for instance, by no means established that "after an epileptiform convulsion the hypoglycemia has achieved its maximum therapeutic effect" and is "therefore an indication for termination regardless of the time at which the seizure intervenes." If the epileptiform convulsion had such a "maximum therapeutic effect" the patients with the greatest number of convulsions ought to have the best prognosis. This is by no means in accord with clinical experience. But Sakel merely announces his theories, without quoting his experience.

The clinician will profit from reading the monograph, provided he ignores the theoretic and considers only the factual part of the exposition.

**The Hypothalamus: Morphological, Functional, Clinical and Surgical Aspects.** By W. E. Le Gros Clark, John Beattie, George Riddoch and Norman M. Dott. Price, 12 s., 6 d. Pp. xii + 213, with 104 figures. Edinburgh: Oliver and Boyd, 1938.

Four lectures delivered at the University of Edinburgh, under the auspices of the William Ramsay Henderson Trust, are assembled in this book. The first lecture, by Le Gros Clark, entitled "The Morphological Aspects of the Hypothalamus," presents an excellent and authoritative account of the structure and connections of this part of the brain. The supraopticohypophysial tract, joining

the hypothalamus with the neural division of the hypophysis, is described briefly. The author unfortunately adheres to the view of Popa and Fielding that a portal circulation carries blood from the hypophysis to the hypothalamus, in spite of the evidence to the contrary presented by Wislocki.

The second lecture, by Beattie, is devoted to the functional aspects of the hypothalamus, and hypothalamic activity is considered from the point of view of its role in the regulation of the constancy of the internal environment, and particularly in the regulation of body temperature.

In the third lecture, by Riddoch, are considered in a none too satisfactory manner the clinical aspects of hypothalamic derangement.

The concluding lecture, by Dott, on the surgical aspects of the hypothalamus contains accounts of the technical procedures involved in operating in cases of epidermoid hypophysial tumors of the third ventricle, which illustrate well the surgical approaches to the hypothalamic region. The clinical features of these cases are presented in some detail, and the remaining portion of the lecture is devoted to the signs of hypothalamic derangement encountered in surgical practice, based in large part on hitherto unreported cases from Dott's clinic. A wealth of interesting and informative material is presented and discussed. This section and the initial section by Le Gros Clark are the outstanding features of the book.

**Beitrag zur Kenntnis sklerosierender Entmarkungsprozesse im Gehirn, mit besonderer Berücksichtigung der diffusen Sklerose.** By L. Einarson and A. V. Neel. Acta Jutlandica, Aarsskrift for Aarhus Universitet X, 2. Copenhagen: Einar Munksgaard, 1938. Pp. 144, with bibliography and illustrations.

The authors define diffuse sclerosis as a primary, progressive process of demyelination and sclerosis, which takes place in the white matter of the two hemispheres equally or to different degrees, which ordinarily spares the cortex and arcuate fibers and in which the details of the reaction, especially in the glia, display marked variations. They recognize the following forms: (1) that with glioblastomatous reaction; (2) that with inflammatory reaction (Schilder); (3) the nonfamilial, sporadic, degenerative types (*a*) with fatty products, (*b*) with metachromatic-basophilic products and (*c*) with persistent islands and stripes of myelin; (4) the heredodegenerative, familial types, including (*a*) the acute infantile (Krabbe), (*b*) the subacute juvenile (Scholtz), (*c*) the adult (Ferraro) and (*d*) the chronic (Pelizaeus-Merzbacher), and (5) leukoencephalopathia concentrica (Baló).

After discussing some other classifications and miscellaneous cases, they conclude: "A division of types which suits every one cannot now be given, in view of the incomplete knowledge of the etiologic factors and the pathogenesis in individual cases."

The authors report in detail 4 cases obviously belonging in the general category and 2 more doubtful ones. They are inclined to believe that some at least of the lesions studied are of thrombotic origin, but they review other theories which have been proposed. They suggest that the disease may be due to a constellation of factors, such as a lack of vitamins (especially E) and a hereditary tendency to one or another form of glial reaction. There is an excellent bibliography.

**Zur Entdeckung der Insulinschocktherapie bei akuten Geisteskrankheiten, insbesondere bei der Schizophrenie.** By Dr. Julius Schuster. Price, 2 pengös. Pp. 90. Budapest, Hungary: Druckerei der Pester Lloyd-Gesellschaft, 1938.

Essentially, this booklet is a claim for priority. As early as 1923 the author treated a number of patients with conditions classified as dementia praecox, cryptogenic epilepsy and manic-depressive psychoses with large doses of insulin. In 1926 he gave a preliminary report before the medical society of Budapest and published his results in 1928 in the *Archiv. für Psychiatrie und Nervenkrankheiten.* The

highest dose mentioned is 160 units. He produced hypoglycemia and coma. The occurrence of convulsions is not mentioned. Brief abstracts of 30 cases are given. It is not stated whether these cases represent a mere sample or the total number of patients treated. On the basis of these facts the author states that "insulin therapy is erroneously credited to Sakel: I should be given priority for insulin therapy of psychoses" *(Fälschlich wird daher die Therapie mit Insulin Sakel zuerkannt, die Priorität der Insulintherapie der Psychosen gehört mir).*

The greater part of the book is given over to a highly technical discussion of the biochemistry of insulin action. The clinical part is practically limited to a sketchy description of the 30 cases already mentioned. The biochemist might derive benefit from reading the treatise. To the clinician it is of little value.

**The Principles and Practice of Perimetry.** By Luther C. Peter. Price, $4.50. Pp. 331. Philadelphia: Lea & Febiger, 1938.

This is the fourth edition of this standard manual on the principles and practice of perimetry. It is comprehensive and is a valuable addition to the neurologist's library of essential information.